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ACTA RADIOLOGICA

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ACTA RADIOLOGICA
EDITA IUSSU SOCIETATUM RADIOLOGICARUM
DANIAE, FENNIAE, NORVEGIAE ET SUECIAE

VOL. 40 DECEMBER 1953 FASC. 6

ANGIOGRAPHIC DETERMINATION OF TUMOUR PATHOLOGY

by

Ingmar Wickbom

The possibility of establishing a differential diagnosis of tumours by the aid of angiography is mainly based on the fact that many tumours have a vascular supply and architecture different in appearance from the vascularity of the normal brain tissue.

The differences are, perhaps, most marked when the tumour is highly vascular and contains numerous pathologic vessels. But some tumours are poor in vessels compared to the surrounding tissue while other tumours undergo degenerative changes and contain necrotic parts, cysts or haemorrhages. In the angiographic examination, such parts of a tumour come out as poorly vascularized regions, while other parts of the tumour may be rich in vessels. For the determination of an actual species of tumour there are, however, several other factors to consider, such as the manner of growth and the situation. Some tumours are expanding. In their growth they push away adjacent brain tissue and thus cause considerable displacement of vessels. Others infiltrate the brain and, therefore, do not cause displacements of the same kind. Such tumours may, on the other hand, grow around the vessels and give them a stretched appearance. As to the situation, this is of special importance in the pathologic diagnosis, particularly for differentiating between extracerebral and intracerebral tumours. It is possible, in many cases, to establish from the situation of the tumour that its position must be intracerebral. The alternative diagnosis of meningioma may then be practically eliminated. It is of the greatest importance, for the establishment of a pathologic diagnosis,

Submitted for publication, March 4, 1953.

This paper is a more complete treatment of the subject dealt with in a lecture given at the second Symposium Neuroradiologicum, Rotterdam 1949.

From the Roentgen Department (Director: Professor ERIK LINDGREN), Serafimerlasarettet, Stockholm, Sweden.

to determine exactly the position of a tumour in relation to the brain substance — whether it is extracerebral, intracerebral or intraventricular. In this respect, pneumography generally supplies more accurate information, especially about the position of the tumour in relation to the ventricular system. It should therefore be used when the nature of the tumour cannot be determined by angiography alone.

I have studied about 500 cases of tumours subjected to angiography with the object of forming an opinion about the nature of the vascular changes and the frequency with which they occur with different types of tumours. Table I shows the rate of occurrence for the various types of tumours in the material. In most cases, they have been verified at operation or autopsy. A few cases which had angiographic changes characteristic of glioblastoma were not operated upon. These cases were nevertheless included in the material, the diagnoses being regarded as definite on the strength of the angiographic evidence combined with the clinical picture. Had these tumours been excluded from the material the statement as to the rate of occurrence of the various types of vascular changes would have been misleading.

Table 1

Material

Glioblastomas	243	cases
Astrocytomas	77	»
Oligodendrogliomas	25	»
Other gliomas	15	»
Meningiomas	85	»
Metastases	40	»
Tuberculomas	6	»
Abscesses	20	»
Haematomas	10	»
Total	521	cases

The types of tumours most frequently supplied with pathologic vessels are glioblastomas, meningiomas and metastases. Truly pathognomonic changes occur, however, only with the two first types, but just for those types is it particularly valuable to obtain a definitive preoperative pathologic diagnosis, since this may influence the indications for operation or the planning of the operation. Meningiomas, because of their usually benign character and because they do not infiltrate adjacent brain tissue, are gratifying objects of operation. On the other hand, with the very malignant and as a rule poorly delimited glioblastomas, a radical removal is often technically impossible and the rate of recurrence is very high. An operation can as a rule only postpone the fatal ending.

In the main, I shall therefore restrict my discussion to the vascular changes occurring with these two types of tumours, starting with the

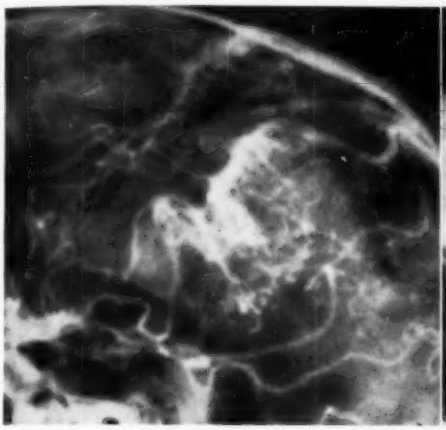


Fig. 1.

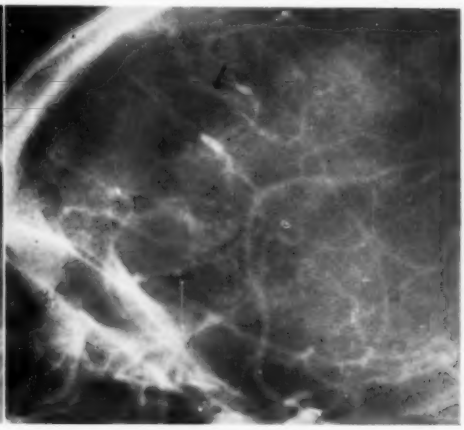


Fig. 2.

Fig. 1. Parietal glioblastoma. Vascular changes — type I. The tumour contains numerous irregularly coursing vessels of varying lumen. The fact that several veins are contrast-filled already in the arterial phase indicates arteriovenous fistulas.

Fig. 2. Frontal glioblastoma. Vascular changes — type I. There are several arteriovenous fistulas but only a few irregular vessels that are contrast-filled.

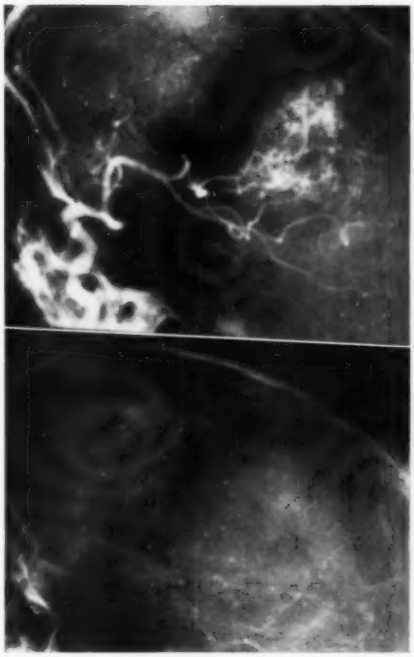


Fig. 3. Rapid circulation in the tumour due to arteriovenous fistulas. Below: 1—2 seconds after the termination of the injection, hardly any contrast remains in the tumour.

glioblastomas. These I have divided into 6 groups, on the basis of the vascularity of the tumour as it appears at angiography.

Table 2

Glioblastomas

Type I	74	cases	(4)
» II	30	»	(1)
» III	22	»	(7)
» IV	59	»	(10)
» V	28	»	(11)
Normal vascularization	30	»	
	Total 243	cases	(33)

Group I. The characteristic feature is that contrast-filled veins are observed in the arterial phase, when only arteries are filled in other parts of the brain. This is due to direct connections (so called arterio-venous fistulas) between arteries and veins, no intermediate system of capillaries being present. Apart from the fistulas, the tumour generally contains plenty of irregularly coursing vessels, the lumen of which varies (Fig. 1). In exceptional cases, however, there are only a few vessels of the kind just mentioned (Fig. 2).

When the number of fistulas is great, the contrast medium passes rapidly through the tumour. Thus, in some cases, the medium may have almost entirely disappeared from the tumour in the venous phase (Fig. 3). In such a case it may be difficult to make a diagnosis other than arterio-venous aneurysm when direct connections between arteries and veins also occur. In other cases again, the medium may pass rapidly through the arteries, but stagnate in the veins, which may be contrast-filled when

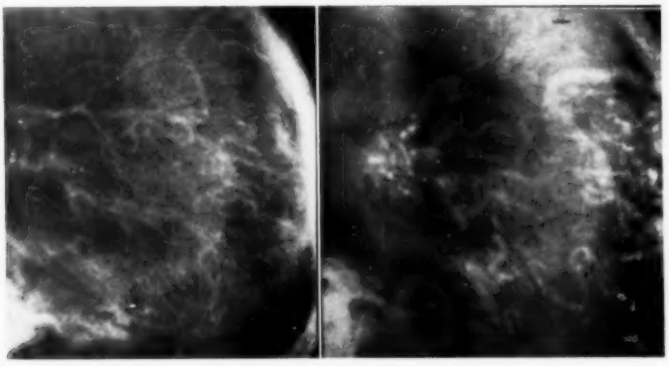


Fig. 4. Glioblastoma in the parieto-occipital region. The contrast passes rapidly through the tumour but has stagnated in the veins though other parts of the brain are emptied of contrast.

other parts of the brain are emptied of contrast (Fig. 4). This may be due partly to constricted vessels and partly to oedema in and around the tumour. In some cases, the tumour vessels may be even better contrast-filled in the venous phase than in the arterial phase.

Except for cases of glioblastomas and arterio-venous aneurysms it is only with the very rare, so called malignant meningiomas, that contrast-filled veins are observed in the arterial phase. But in cases of malignant meningiomas, the other tumour vessels are as a rule more regular and the tumours moreover obtain part of their blood supply from the external carotid artery. This was observed at least in the few cases we have investigated.

Contrast-filled veins indicating arterio-venous fistulas were found in 74 out of the 243 glioblastoma cases.

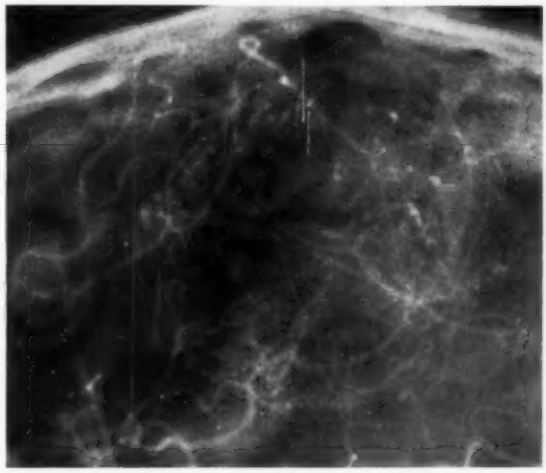
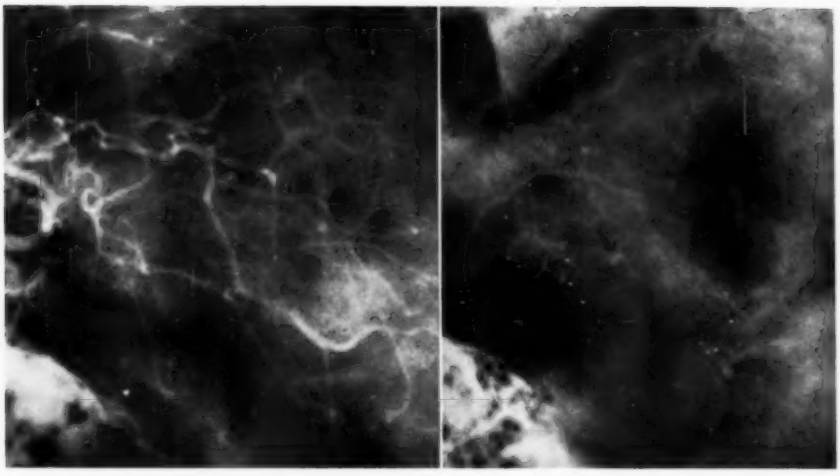


Fig. 5. Glioblastoma in the parietal lobe, illustrating type II changes. Abundance of irregular vessels in the tumour, of the same type as in group I. The arterial phase shows, however, no contrast-filled veins.

Group II. The vascular changes occurring in this group are demonstrated in Fig. 5. Irregular tumour vessels of similar appearance to those of the preceding group are present in abundance, but no contrast-filled veins indicating arterio-venous fistulas are seen in the arterial phase. Changes of this kind were observed in 30 glioblastoma cases. The changes are, however, not pathognomonic of glioblastoma since they occur occasionally also with metastases. In our material, such changes occurred in 2 out of the 39 cases of metastases.



a. b.

Fig. 6. Glioblastoma in the temporal lobe. Vascular changes of type III. Some short irregular vessels with small aneurysmal dilatations (↓) are seen in the tumour region.

Group III. The tumours of this group also contain many tumour vessels but the vessels are shorter and less wide than in the foregoing groups. Their lumen is, however, irregular with small aneurysmal dilatations (Fig. 6).

Changes of this kind were observed in 22 cases of glioblastoma. However, similar changes were seen in 6 out of the 39 cases of metastases. The probability of metastases is greater, therefore, in this type of change than in the one occurring in the preceding group.

Group IV. In cases belonging to this group, only some short comparatively thin vessels with slightly irregular lumen are seen in the tumour region (Fig. 7). It is sometimes difficult to distinguish between these and fragmentarily filled normal vessels, especially the so-called striothalamic vessels from the anterior choroidal artery (Fig. 8). Tumour vessels of this appearance are not characteristic for any specific type of tumour but occur with glioblastoma as well as with other kinds of glioma, and occasionally with metastases. Similar vessels may occur in meningiomas but then usually have a more regular arrangement. Changes of the kind now described were present in 59 cases of glioblastoma.

The changes discussed in the foregoing represent the four types of newly-formed vessels that occur with glioblastoma. However, haemor-

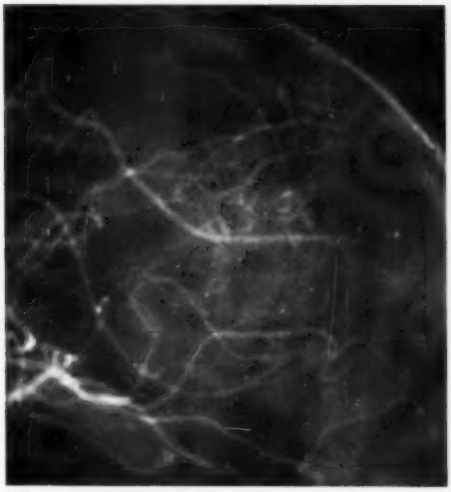
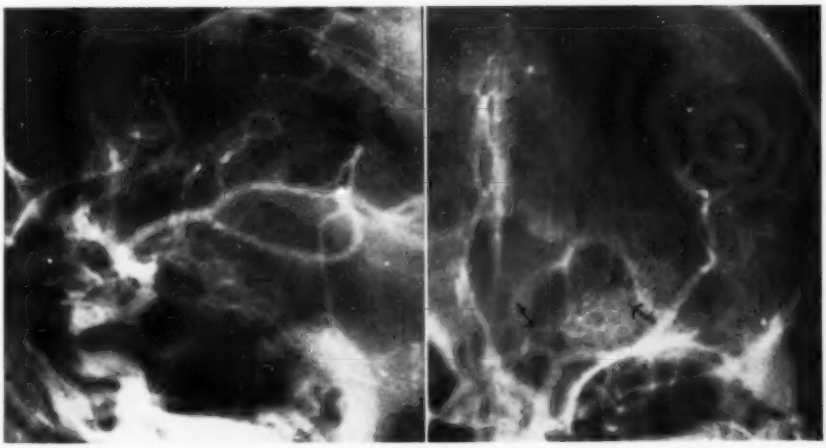


Fig. 7. Glioblastoma in the parietal lobe. Vascular changes of type IV. Only some short slightly irregular vessels are seen in the tumour.

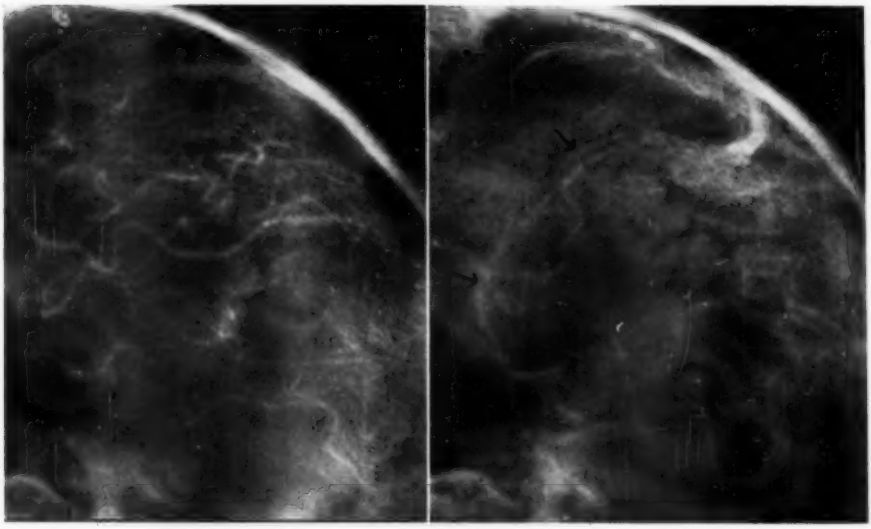


a. b.

Fig. 8. The small vessels with twisted courses (→) are not tumour vessels but normal branches from the anterior choroidal artery (↓).

rhages and degenerative changes in the form of necroses and cysts are often present with glioblastoma; the angiographic picture will then be different. Since there are no vessels in those regions, they appear on angiography as almost non-vascular areas, surrounded by a usually ring-formed, more

Fig. 9. Glioblastoma type I in the parietal lobe. The centre of the tumour is almost completely free from vessels, due to degenerative changes.



a. b.

Fig. 10. Glioblastoma of type I in the parietal lobe. The tumour is poorly vascularized but in the periphery some small irregular vessels and arched veins (→) are seen in the venous phase.

or less vascular, zone. (Vessels in the vicinity may be projected over the non-vascular area, causing it to appear not completely devoid of vessels.) Haemorrhages and such degenerative changes may be present in all the

groups. Four cases were found in group I (Fig. 9), one case in group II, seven cases in group III and ten cases in group IV. The highest rate of occurrence thus corresponds to the two groups where the vascular changes are less typical. Especially in these two groups, they are generally best seen in the venous phase.

Yet, the presence of a non-vascular area with a peripheral, highly vascular zone is not in itself pathognomonic of glioblastoma, since similar changes also occur with other types of glioma as well as with metastases. But they are rarely found except in cases of malignant tumours. It is also true that a circular, highly vascular zone around a non-vascular area may be observed in cases of meningioma, although the peripheral vessels then have a much more regular appearance. With abscesses, a non-vascular area surrounded by a highly vascularized zone is often seen; the peripheral vessels, however, have no irregular lumina, but appear as normal brain vessels. Occasionally, if the abscess is of long standing, a circularly coursing vein may be observed to surround the non-vascular area.

In 28 cases, clear evidence was found that the tumour region was poorer in vessels than the surroundings. In 11 of these, the venous phase showed the tumour to be partly surrounded by short, arched vessels (Fig. 10), whereas in the 17 remaining cases, no peripheral tumour vessels were found.

In 30 cases, it was not possible angiographically to demonstrate any conspicuous change in the architecture of the vessels. Thus, the possibility of glioblastoma cannot be excluded, even if the tumour is poor in vessels or has an apparently normal vascular structure. In such cases, angiography can make no important contribution to the pathologic diagnosis.

Meningiomas are usually comparatively rich in vessels. Pathologic vessels were present in about half of our cases. But the vascular architecture shows more regularity than in cases of glioblastoma. Frequently, the newly-formed vessels have a twisted or serpentine course, but their lumen is not as irregular as is characteristic for the glioblastomas.

Table 3

Meningiomas

Type I	24	cases
» II	16	»
» III	6	»
» IV	7	»
Normal vascularization	31	»
Total	84	cases

It is possible, also in cases of meningioma, to distinguish between various types of vascular changes. The most common type is demonstrated in Fig. 11 (type I in Table III). Due to a great abundance of capillaries, the tumour appears as a contrast formation of homogeneous density,

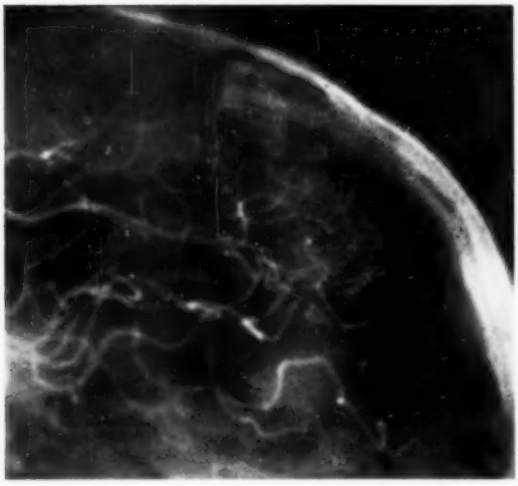


Fig. 11. Meningioma in the parietal region, parasagittally situated. Vascular changes — type I. The tumour is almost homogeneously stained with contrast due to the abundance of capillaries (→).

with sharply delimited and smooth boundaries. As a rule, this 'accumulation' of contrast in the tumour remains also in the venous phase. In many cases it may be seen already in the arterial phase, but occasionally it can be seen in a late phase only (Fig. 12). In the arterial phase there may be either no vessels at all, or a few thin and tortuous but regularly arranged arteries may be contrast-filled. The whole tumour is generally contrast-filled in this manner but sometimes only a part is stained after

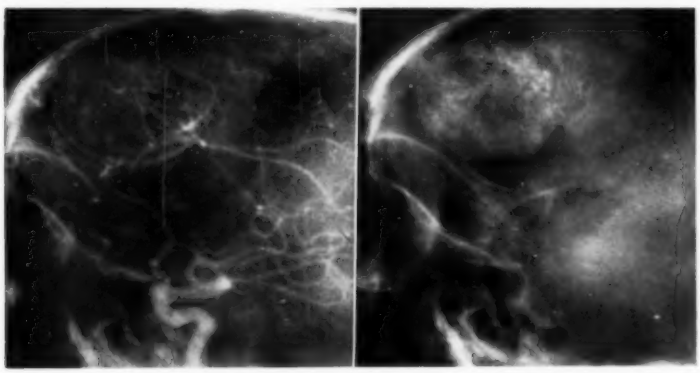


Fig. 12. Meningioma in the frontal region, parasagittally situated. Vascular changes — type I. In the arterial phase, the tumour contains small arteries with twisted courses but a regular arrangement. The tumour is partly surrounded by a bowl-shaped artery. In a later phase the tumour is homogeneously stained.

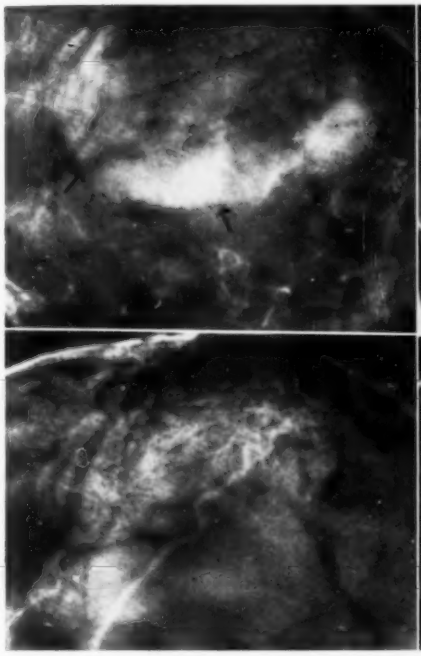


Fig. 13 a and b.

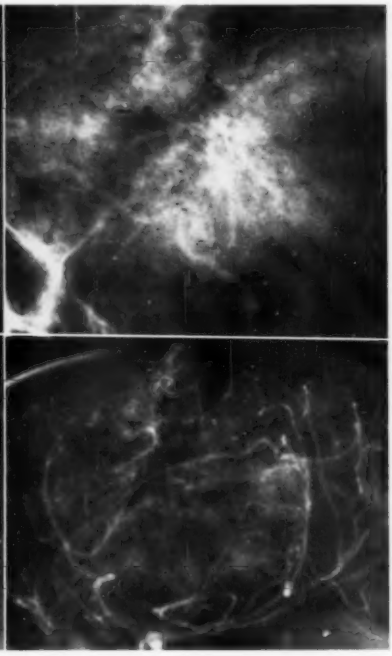


Fig. 14.

Fig. 13. Convexity meningioma in the parietal region. The main part of the tumour is supplied by the internal carotid artery. Below: The upper posterior part of the tumour, however, receives its blood from the external carotid artery.

Fig. 14. Convexity meningioma above the Sylvian fissure. The contrast-filling of the tumour is not very homogeneous after injection into the internal carotid (below) which is due to the fact that the tumour receives blood also from the external carotid (above).

injection into the internal carotid artery. An example of such a tumour case is illustrated in Fig. 13. The contrast formation demonstrated in Fig. 13 a has not the usual rounded shape, the reason being that part of the tumour is supplied from the external carotid artery (Fig. 13 b).

In other cases again, those parts of the tumour that are supplied respectively from the internal and external carotid arteries intermix and the filling of the tumour will not be very homogeneous, if the two arteries are injected separately (Fig. 14).

There are two alternative ways of establishing whether the blood supply to the lesion is derived from both the internal and the external carotid artery: either by making separate injections into these two arteries

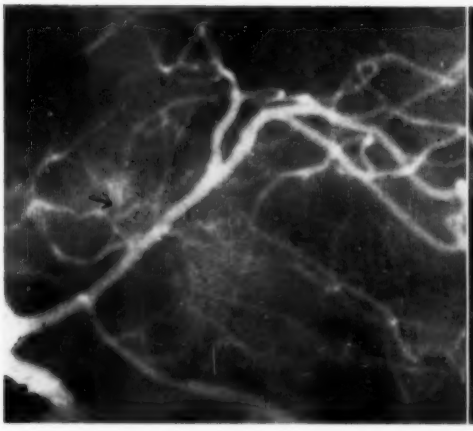
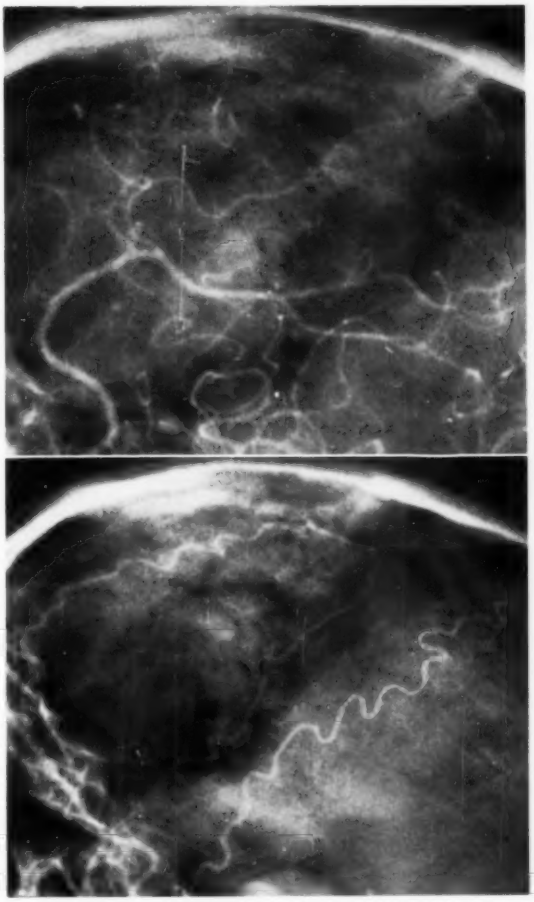


Fig. 15. Meningioma arising from the sphenoidal ridge. The tumour contains small arteries with twisted courses. They have a more regular arrangement than tumour vessels occurring with glioblastomas and the width of their lumen is more uniform.

Fig. 16. Meningioma, the size of a small plum, arising from the posterior part of the sphenoidal plane. Small arteries with a regular arrangement radiate to the centre of the tumour (→).

or by puncturing only one of the arteries in combination with a puncture of the common carotid artery. Whenever it is possible technically to make separate injections into the internal and the external carotid arteries we prefer this procedure.

In 24 out of the 84 meningioma cases in the material, a more or less homogeneously dense contrast-filling was obtained. Statements may be found in the literature to the effect that a homogeneous contrast-filling is pathognomonic of meningioma. Unfortunately, the circumstances are not as favourable as that. A homogeneously dense contrast-filling may also be obtained in cases of tumour metastases (in our material it was observed in 6 of the cases investigated). This is the more regrettable, since the operative indications are essentially different for the benign meningiomas and the malignant metastases. Certainly, it may be possible in some cases to differentiate between meningioma and metastasis, even when the contrast-filling is of homogeneous density. The metastases sometimes have a more irregular, somewhat polycyclic contour and if the filling is obtained in a late phase, the arterial phase may show some vessels that are more irregular than those usually occurring with meningiomas (Fig. 21). Of course, when multiple tumours are observed, this makes the presence of metastases more probable but it can also happen that meningiomas are multiple. On the other hand, the presence of a meningioma may with



a.

b.

Fig. 17. Parasagittal meningioma of central third. No tumour vessels are filled after injection into the internal carotid. The branches from the external carotid to the tumour region are however wide and tortuous. Some thin tumour-vessels with twisted courses are contrast-filled from these branches.

practical certainty be eliminated, if the localization of the tumour definitely indicates an intracerebral position.

The changes described in the foregoing group are due to the unusually rich development of the capillary network in the tumour. In other cases, the changes in vascularity may be due to newly-formed arteries (Cf. type II in Table III). As a rule, these newly-formed vessels are narrow

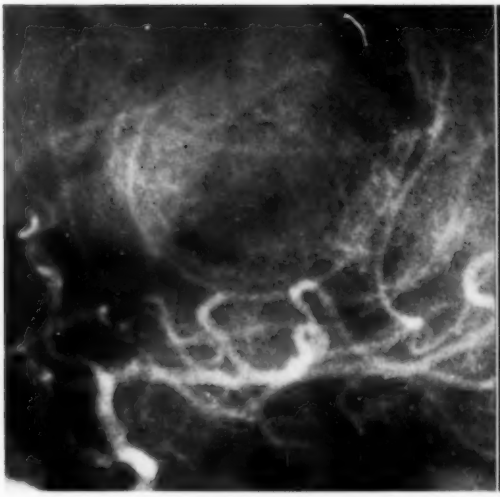


Fig. 18. Convexity meningioma above the Sylvian fissure. There are no distinctly characteristic vessels in the tumour. The tumour is, however, partly encircled by two branches of an ascending artery forming a sort of bowl in which the tumour seems to be embedded.

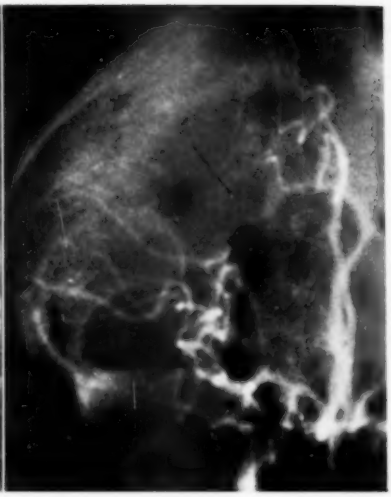


Fig. 19. Meningioma in the Sylvian fissure. There are no definite tumour vessels. The vessels in the Sylvian fissure are displaced away from a semicircular formation having its base against the vault of the skull. This indicates a process lying close to the vault, probably extracerebral.

and follow a serpentine course. They differ from newly-formed vessels in glioblastomas in that they have a regular lumen and show no local strictures or dilatations. Another characteristic feature is that they are often arranged in a broom-like fashion (Fig. 15) or show a radial formation suggesting a wheel (Fig. 16). Changes of this kind were present in 16 of the meningioma cases.

The tumour may sometimes contain a few small, newly-formed vessels with appearances that have no characteristics in common with any specific type of tumour. If it can be demonstrated that such vessels are contrast-filled by an injection into the external carotid artery, the diagnosis of meningioma is fairly certain. The demonstration of an obviously widened and unusually tortuous branch, going to the tumour region, is also sufficient for the establishment of a diagnosis of meningioma. It should be kept in mind, however, that also in normal cases the superficial temporal artery in particular may show considerable variations in caliber. Definite evidence of blood supply from widened branches of the external carotid artery was obtained in 6 cases (Fig. 17), though tumour vessels of specific characteristics were not present (Cf. type III in Table III).

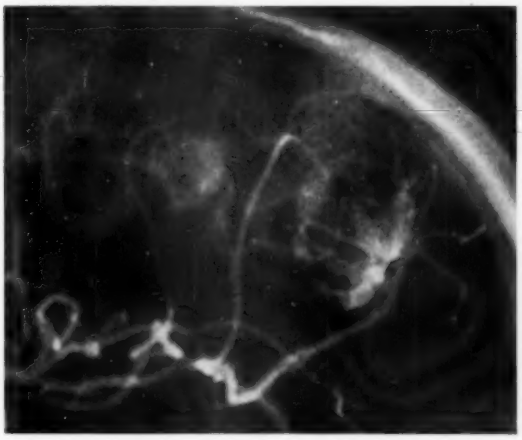


Fig. 20. Multiple metastases in the parietal lobe. The tumours are almost homogeneously stained with contrast, already in the arterial phase. Thus they cannot be distinguished from meningiomas only by their vascular appearance. Multiple tumours, however, are as a rule metastases though primary tumours may occasionally occur in multiples.

The vessels around a meningioma often show such a typical arrangement that a pathologic diagnosis is possible, even if it cannot be demonstrated with certainty that the tumour proper contains newly-formed vessels. The case illustrated in Fig. 18 shows the tumour to be partly encircled by a conspicuously wide artery, forming a sort of bowl in which the tumour lies. It is true that circularly coursing vessels may be found to surround gliomas and metastases as well but these vessels are usually veins, not arteries. What is more, in cases of gliomas and metastasis, it is usually not one single vessel but several small vessels which together form this more or less complete circle around the tumour.

Arteries in a bowl-shaped arrangement around the tumour, in which no definite tumour vessels were present, were observed in 7 of the cases included in the material (Cf. type IV in Table III). Arteries in such an arrangement around the tumour were found also in some of the cases where tumour vessels were observed.

With the exception of the rather rare intraventricular types, the meningiomas practically always are extracerebral tumours. If the vascular displacement indicates that the tumour lies close to the bone, with its base against it, it may be concluded with a fair degree of certainty that it is a meningioma, even if it cannot be demonstrated that there are characteristic tumour vessels or that the vascular supply is derived from the external carotid artery (Cf. Fig. 19). This is especially so when the tumour is confined to one of the sites for which meningiomas are known to show predilection.

Metastases also quite frequently have a pathological vascular supply. Out of the 39 verified metastases in this material, a pathologic vascularity

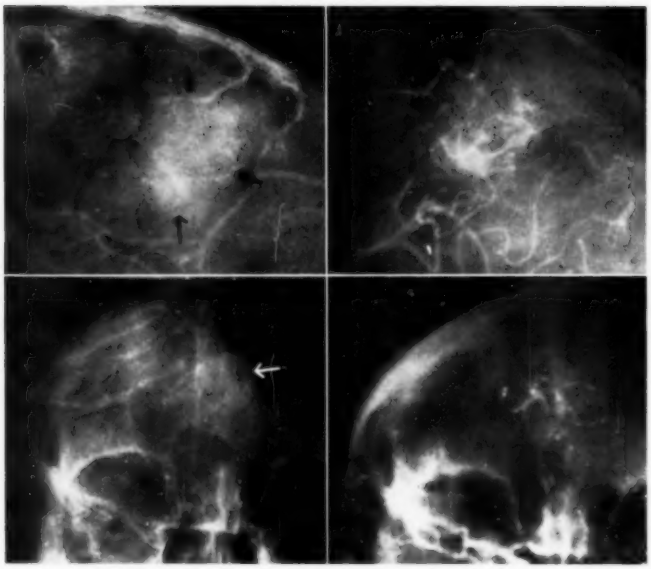


Fig. 21. Hypernephroma metastases close to the midline. In the venous phase the tumour is almost homogeneously stained (→). It is, however, polycyclically outlined and in the arterial phase small vessels are filled and are more irregular than usually observed with meningiomas.

could be demonstrated in 19 cases (Cf. Table IV). The vascular changes, hovewer, vary within wide limits.

Table 4

Metastases

Type I	6	cases
» II	3	»
» III	2	»
» IV	8	»
Normal vascularization	19	»
Total	38	cases

In certain cases, they remind one of the changes found with glioblastoma, whereas in other cases one may see a more or less homogeneous contrast density of the same kind as is often observed with meningiomas.

In 6 of the metastases, a change of the latter kind, *i. e.* with a homogeneous contrast density, was found (type I in Table IV). In these cases it is not possible on the sole basis of the vascular architecture to differentiate them from meningioma. As was mentioned before, however, the

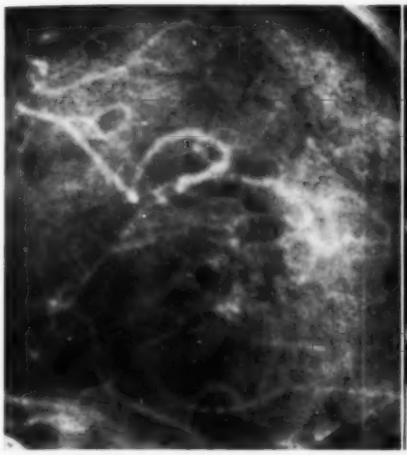


Fig. 22. Carcinoma metastases in the parietal lobe. In the tumour there are irregular vessels of similar appearance as demonstrated with glioblastoma, type III.

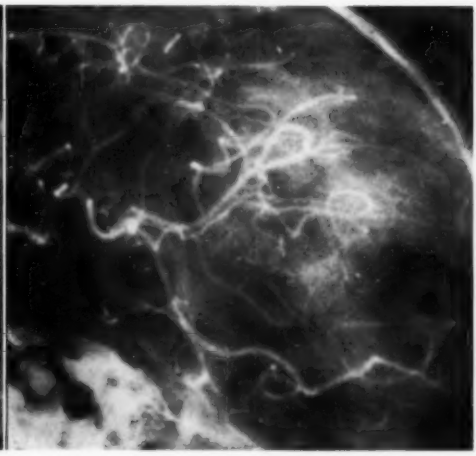


Fig. 23. Hypernephroma metastases in the parietal lobe. Some small irregular vessels similar to those appearing with glioblastomas of type IV are seen in the tumour.

metastases are quite often polycyclically outlined (Fig. 21) while the meningiomas practically always have a smoothly rounded contour. Small irregular vessels may also sometimes be seen in an early phase with metastases but these are usually more irregular in arrangement and their lumen is more variable as compared to similar vessels occurring with meningiomas. Furthermore, the metastases differ from the meningiomas in that they are usually intracerebral. One can be fairly certain that a tumour of the appearance described must be a metastasis, if the localization indicates an intracerebral position.

In 2 cases of metastasis, the tumour had numerous wide and tortuous, irregular vessels of about the same appearance as was earlier described for glioblastomas of type II (Fig. 22 type III in Table IV).

In 8 cases, some small, tortuous and somewhat irregular tumour vessels were contrast-filled, similar to those occurring with glioblastomas of the types III and IV (Cf. type III in Table IV). It is not possible in such cases to draw any definite conclusions as regards the nature of the tumour merely from the appearance of the tumour vessels (Fig. 23). However, tumours of this appearance are usually malignant (glioblastomas or metastases).

Haemorrhages and degenerative changes may occur also with metastases. If the tumour is highly vascular, one may find similar changes as

those described earlier for glioblastoma, for instance a poorly vascular region surrounded by a more or less vascularized zone. Changes of this kind were present in 3 of our cases.

SUMMARY

The vascular changes occurring in glioblastomas, meningiomas and metastases are described and their frequency in a material of about 500 tumour cases is reported. The angiographic appearances are discussed with special reference to the differential diagnosis.

ZUSAMMENFASSUNG

Die bei Glioblastomen, Meningiomen und Metastasen auftretenden Gefässveränderungen werden geschildert; über ihre Häufigkeit in einem Material von etwa 500 Tumorfällen wird berichtet. Das angiographische Aussehen der Veränderungen wird unter besonderer Berücksichtigung der Differentialdiagnose besprochen.

RÉSUMÉ

L'auteur décrit les modifications vasculaires qui surviennent dans les glioblastomes, les méningiomes et les métastases et indique leur fréquence dans un matériel d'environ 500 cas de tumeurs. Il étudie leurs aspects angiographiques, en particulier au point de vue du diagnostic différentiel.

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FROM THE ROENTGEN DEPARTMENT I (DIRECTOR: DOCENT GUNNAR JÖNSSON),
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ANGIOCARDIOGRAPHIC DEMONSTRATION OF PULMONARY STENOSIS

by

Gunnar Jönsson, Bror Brodén and *Johan Karnell*

The difficulty, not to say impossibility, of visualizing the outflow tract of the right ventricle and the pulmonary valves by intravenous angiocardiography is sometimes pointed out in the radiologic and cardiologic literature. In the June 1953 number of Radiology, SUMNER N. MARDER and WENDELL G. SCOTT mention this difficulty and recommend the right anterior oblique view. The introduction to their paper clearly expresses the opinion generally held and we therefore cite it here. "At the present time, pulmonic stenosis is the most important single criterion in the evaluation of patients with cyanotic congenital malformations of the heart for the selection of those who may benefit from surgical measures. Furthermore, the accurate delineation of the infundibular portion of the right ventricle by angiocardiographic study may be of value in determining whether an aorticopulmonary anastomosis or an infundibular resection be undertaken. DOTTER and STEINBERG have recently estimated that pulmonic stenosis is directly visualized in only one-half the cases of the tetralogy of Fallot. COOLEY and his coworkers have also reported that in many of these cases angiocardiography has provided only indirect evidence of pulmonic stenosis." SOULIÉ, CHICHE and VOCI also considered that a diagnosis of infundibular pulmonary stenosis must be based on indirect signs. In their more recent publications, however, SOULIÉ and his coworkers state that selective angiocardiography will provide direct information.

With regard to the tetralogy of Fallot, GOODWIN, STEINER, MOUNSEY, MACGREGOR and WAYNE write as follows: "Failure to visualize the type and site of the pulmonary stenosis in more than 20 per cent of the cases is a serious defect of this method of angiocardiography, particularly

Submitted for publication, Sept. 17, 1953.

in cases where pulmonary valvulotomy is planned. It is probable that more elaborate techniques may enable the stenosis to be accurately demonstrated in a larger proportion of cases." In connection with this, reference is made to a paper on selective visualization in angiocardiography.

Many other opinions similar to these might be added, but those mentioned already are perhaps sufficient. The views reflected in these statements may be summed up in the following three points.

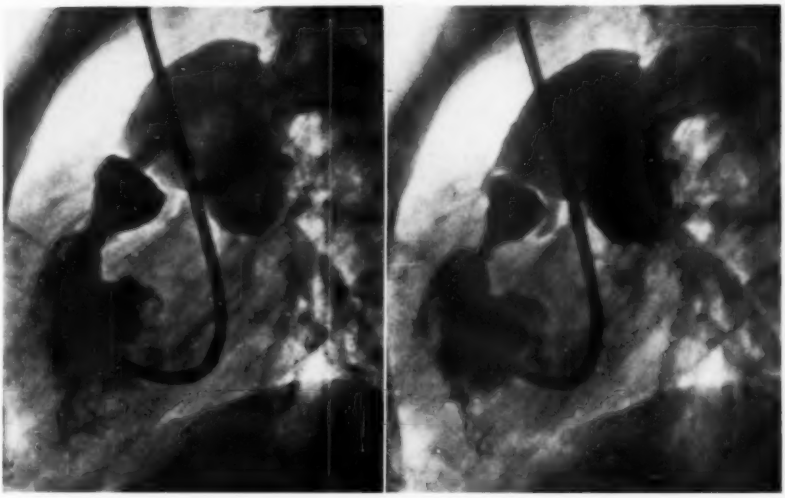
1. Angiocardiography after intravenous injection of a contrast medium is a defective method for visualizing the pulmonary conus and valves in cases of pulmonary stenosis.
2. There is a definite need for an angiocardiographic method that will enable an accurate delineation of these areas.
3. Selective angiocardiography is sometimes suggested for this purpose, but some hesitation seems to be felt in using it.

The cause of this hesitation is not quite clear, but in all probability there are two main reasons.

In the first place, to inject a contrast medium directly into the right ventricle is probably considered dangerous. To meet this it may be said that the injection of a contrast medium of the type commonly used (Umbradil, Diodrast, Perabrodil, etc.), as well as the introduction of a catheter, always involves some risk. Accidents seldom occur, however. Since 1948 we have carried out over one hundred selective angiocardiographies with injection into the right ventricle without any serious complications occurring. KJELLBERG has used the same method with equally good results in about 150 cases. Selective angiocardiography therefore does not seem to be more dangerous than any other method for examination of the heart with a contrast medium.

Another possible objection to the method might be the fear that it is troublesome and time-consuming to perform. This is erroneous. If it is done immediately after the catheterization, which must in any case be carried out for clinical purposes, it takes but 10—15 minutes. The only difficult part of the technique is to learn how to inject so that the catheter will remain in position and not recoil from the ventricle and out into the auricle. This does not take long to master, and in any case, this difficulty will be obviated as soon as the method becomes so well known that manufacturers consider it worth their while to make special catheters for this purpose, with a hole in the side instead of at the tip. Experiments we have carried out have proved that this type of catheter is less inclined to glide backwards.

There is therefore no reason why selective visualization of the right ventricle and pulmonary artery should not be used in cases of pulmonary



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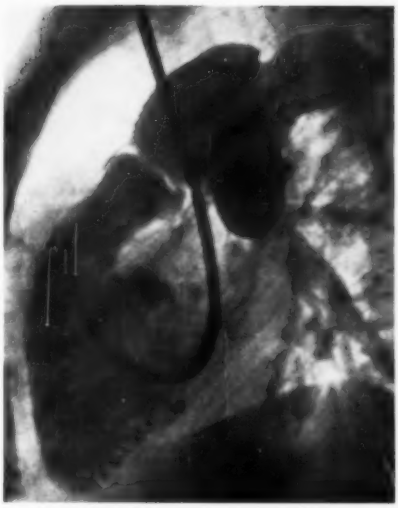
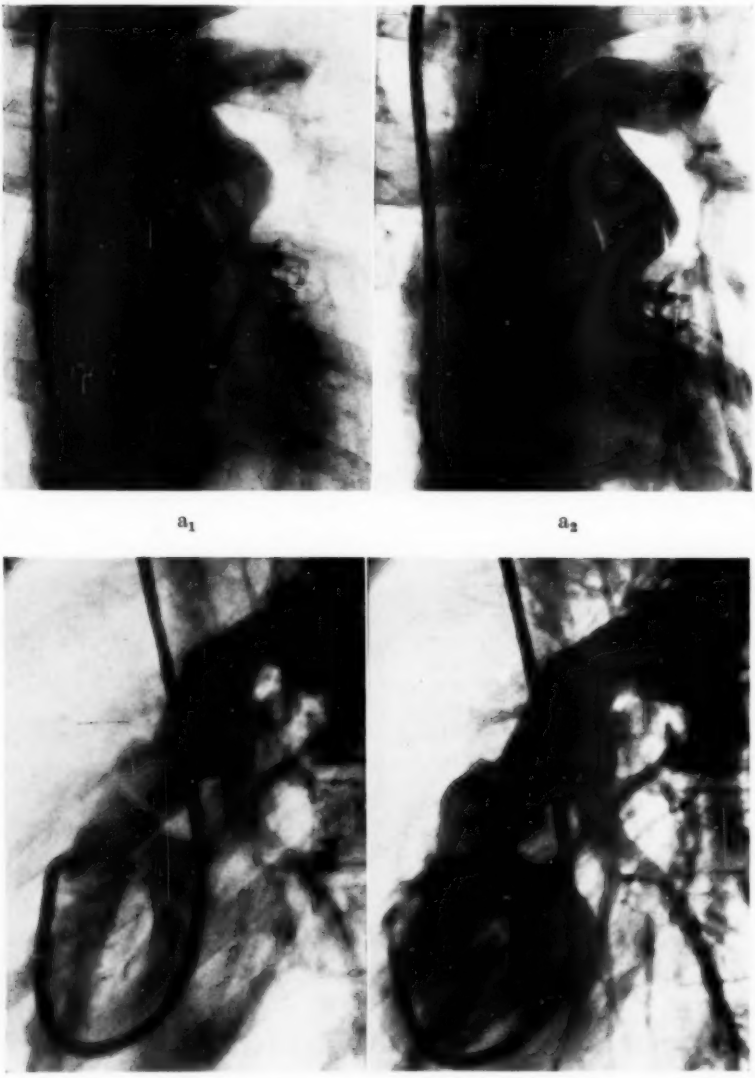


c.

Fig. 1. Valvular pulmonary stenosis and auricular septal defect. Cyanotic 35 years old female. Catheterization disclosed an auricular septal defect and signs of stenosis in the region of the pulmonary valves. 50 cc. of Umbradil 70 % injected (No. 9 F catheter over a period of 3 minutes). The tip of the catheter lay beside the pulmonary valves and during the injection slid down into the middle of the pulmonary conus. Lateral view: The valvular region is narrowed so that only a thin stream of contrast fluid runs into the pulmonary artery (a). The pulmonary artery is dilated. The lumen of the pulmonary conus changes considerably from systole (b) to diastole (c).

stenosis. It is the only method that will give exact information. Intravenous injection should only be used in the rare cases where it is impossible to introduce the catheter into the right ventricle. The injection should then be made into the superior vena cava.



a_1 a_2

b_1 b_2

Fig. 2. Tetralogy of Fallot in a 17 years old male. 65 cc. of Umbradil 70 % injected. a_1 and a_2 frontal views; b_1 and b_2 lateral views. a_1 and b_1 exposed immediately at the beginning of the injection, a_2 and b_2 exposed about 2 seconds later. Enlargement and hypertrophy of the right ventricle, as well as severe infundibular stenosis and a ventricular septal defect. The pulmonary valves are movable but unusually thick.

In selective visualization of the outflow tract and pulmonary artery, the most suitable projections may be selected without any risk of important details being obscured by superimposed opaque medium in vessels or chambers of no interest. In cases of pulmonary stenosis, the outflow tract and pulmonary artery form an arch that lies almost exactly in the sagittal plane. Their anatomy is therefore visualized best in true lateral views. According to ordinary radiologic principles, films should be taken in two planes at right angles to one another. The lateral views should therefore be complemented with others taken in the anteroposterior projection and exposed simultaneously. In those cases in which selective visualization is impossible for some reason and the contrast medium must be injected into the superior vena cava, lateral views are worthless because the outflow tract is obscured by opaque medium in the right auricle. The right anterior oblique projection (actually the left posterior oblique projection, with the patient in the supine position) is the only projection that will furnish informative films in these cases but since the central ray passes obliquely through the infundibulum and the pulmonary valves, these areas will be less distinctly visualized. The opaque medium is, furthermore, more diluted. A direct intraventricular injection is always superior.

As the heart is an organ in continual movement, the films must be exposed in rapid succession. If this is not done, temporary functional states may be interpreted incorrectly as permanent anatomic abnormalities. We use an exposure rate of six per second.

Since all forms of angiocardiography and catheterization involve risks, everything possible should be done to avoid them. During the manipulations with the catheter, particular attention should be paid to whether the ventricle is especially sensitive to the touch of the catheter. If it reacts with greater irregularity than usual to catheterization, and if the patient suffers an undue amount of discomfort, it is wisest to refrain from selective visualization. The injection of contrast medium irritates the myocardium mechanically in the same way as catheterization. In order to reduce the irritability, 120 cc. of a 0.25 per cent solution of ethocaine is injected slowly through the catheter over a period of five or ten minutes, immediately before the injection of the contrast fluid. The final thing that should be done before injecting the opaque medium is to see that the catheter is correctly placed. It should lie with its tip in the upper part of the pulmonary conus, immediately below the valves. One should be absolutely certain that the catheter really is in this position and not in some other heart space or vessel. It should also lie free in the lumen, and the tip should not be caught between trabecular muscles. If the catheter tip is lying free as it should, it will move backwards and forwards a few centimetres during the pulsations. We use a 70 per

cent solution of Umbradil, about 1 cc. per kilogram of body weight. The solution is injected with the aid of a pressure apparatus. The catheter should have as wide a diameter as possible. The rate of injection must be fairly low, not more than 15—20 cc. being injected per second. Electrocardiograms should be taken during the examination.

Conclusions

1. Angiocardiography after intravenous injection is a defective method for examination of the outflow tract of the right ventricle in cases of pulmonary stenosis.
2. If adequate surgical therapy is to be applied exact pre-operative information as to the anatomy is necessary.
3. Selective angiocardiography is the only method that enables the radiologist to supply such information.
4. Selective angiocardiography does not seem to entail any greater risk than other forms of angiocardiography and catheterization. No form of angiocardiography is without risk, and every precaution should therefore be taken.
5. Films must be taken in rapid succession — in adults at a rate of 6 exposures per second, in children perhaps even more rapidly.

SUMMARY

The authors stress the value of selective visualization of the outflow tract of the right ventricle in cases of pulmonary stenosis, giving reasons for their opinion that this method is superior to other forms of angiocardiography.

ZUSAMMENFASSUNG

Die Verf. betonen den Wert der selektiven Sichtbarmachung des Abflussgebietes des rechten Ventrikels in Fällen mit Pulmonalisstenose und begründen ihre Ansicht, dass diese Methode anderen Formen der Angiocardiographie überlegen ist.

RÉSUMÉ

Les auteurs font ressortir l'intérêt de la visualisation sélective de la chambre d'évacuation du ventricule droit dans les cas de sténose pulmonaire et donnent les raisons pour lesquelles ils pensent que cette méthode est supérieure aux autres formes d'angiocardiographie.

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FROM THE ROENTGEN DEPARTMENT I (DIRECTOR: DOCENT GUNNAR JÖNSSON),
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A PERSISTENT LEFT SUPERIOR VENA CAVA COMMUNICATING WITH THE LEFT ATRIUM AND PULMONARY VEIN

by

Per Ödman

A persistent left superior vena cava may be recognized in conventional roentgenograms as a prominent, well-defined paramediastinal bulge below the aortic arch. The vessel may be visualized angiographically if the contrast medium is injected intravenously from the left arm. The vein usually opens into the right atrium or the coronary sinus. This anomaly does not change the normal course of the circulation to any appreciable extent.

However, a persistent left superior vena cava may also communicate with the pulmonary veins or the left atrium, thus abnormally shunting the arterialized blood into the right side of the heart.

If the majority of the pulmonary veins communicate with the systemic veins, large quantities of blood recirculate. This leads, at a very early stage, to deleterious right heart failure and an insufficient systemic supply. The hemodynamics undergo less change if there is a concurrent cardiac malformation, permitting a compensating passage of the blood from the right to the left heart; *i. e.* an auricular septal defect. The prognosis is considerably more favourable under such conditions. SNELLEN & ALBERS have described four cases of this type. Their patients showed only slight hemodynamic impairment, and two of them had reached adult age.

The drainage of only one or a few pulmonary veins into a persistent left superior vena cava, on the other hand, causes no significant disturbance of the circulatory dynamics. This is a very rare anomaly. It is

Read at the Meeting of the Swedish Association of Medical Radiology, May 13, 1953; submitted for publication, June 2, 1953.

principally described from the anatomic point of view, and its clinical and roentgenologic picture is but little known.

Since a persistent left superior vena cava communicates with the left atrium, it usually occurs in combination with other cardiac malformations. (McCOTTER.) In the anatomic literature there are descriptions of this malformation, by GREIFENSTEIN, for example. Moreover, FRIEDLICH et al. published studies of circulatory conditions in four such cases. All were associated with other cardiac malformations. Two of these — one in combination with pulmonary stenosis, the other with an auricular septal defect — were reported to have right-to-left shunts. By intravenous injection from the left arm it was possible to follow the passage of the contrast medium through the left superior vena cava over into the left atrium. In still another of FRIEDLICH's cases, associated with the tetralogy of Fallot, the contrast medium passed in a similar manner centrally through the left superior vena cava. No illustrations from these angiographic investigations were published.

STACKELBERG, LIND & WEGELIUS (1952) described one case of absence of the inferior vena cava. A concurrent persistent left superior vena cava and auricular septal defect were observed. Contrast medium injected intravenously from the left arm passed via the left superior vena cava into the left atrium.

The alterations in the circulatory dynamics vary rather considerably in anomalies of this type, depending upon concurrent complicating cardiac malformations. For this reason each case is of particular interest and it seems desirable to report a case of a persistent left superior vena cava communicating with the left atrium and one pulmonary vein.

The patient, a 14-year-old boy, was referred for coarctation of the aorta. There were no signs of heart failure. He had never been easily exhausted. Examination revealed no cyanosis during rest or exertion. No clubbing was observed. On auscultation a systolic murmur was heard with maximum intensity immediately to the right of the apex.

A roentgenogram of the thorax (Fig. 1) showed a prominent rounded soft-tissue contour paramediastinally to the left, which was partially projected over the aortic arch. The mass appeared to be a persistent left superior vena cava. On the right side, at the level of the hilum, the right superior vena cava bulged laterally more than usual. The central pulmonary vessels were somewhat dilated. Furthermore, erosions of the ribs and deformation of the aortic arch typical of aortic coarctation were observed.

On thoracic aortography a total stenosis in the descending aorta, about three centimeters inferior to the origin of the left subclavian artery, was observed. The pathologic structure paramediastinally to the left was not investigated, as it was regarded at that stage as a relatively irrelevant anomaly.

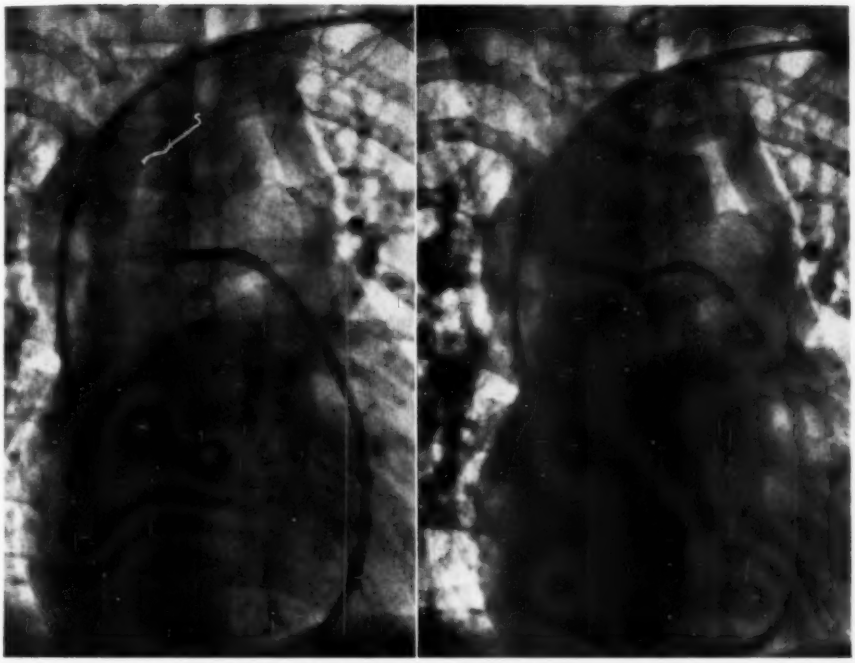
On operation (aortic resection + end-to-end suture), a vein the size of an index finger was encountered to the left in the mediastinum, anterior to the vagus nerve. This was identified as a persistent left superior vena cava. Since its circulatory conditions and topography could not be clarified, nothing was done pending more detailed cardiologic and angiographic investigation.

Fig. 1. Thorax — frontal: Bulging superior venae cavae in the mediastinum bilaterally.

Postoperative right-heart catheterization gave the following results:

	O_2 content vol.%	O_2 saturation
Left innominate vein superior to persistent left sup. vena cava	10.9 %	65.0 %
Right sup. vena cava at level of the manubriosternal joint	13.8 %	81.8 %
Right atrium	14.3 %	84.6 %

The arterial oxygen saturation was 95.6 per cent at rest and 95.0 per cent after exertion. The catheterization study indicated that arterialized blood was entering the systemic veins at some point between the most superior part of the left innominate



a. b.

Fig. 2. Selective angiocardiography: a. Visualization of the anomalous connection between the left atrium and left superior pulmonary vein and left superior vena cava respectively. The left innominate vein and right superior vena cava are beginning to fill with contrast medium. b. A portion of the contrast medium has recirculated abnormally to the systemic vein and right atrium. The left innominate vein and right superior vena cava are dilated (slight filling of the ascending aorta may be seen).

vein and the right superior vena cava, at the level of the manubriosternal joint. However, it was impossible to localize the exact site of entry. There were no indications that blood was abnormally shunted from the right to the left side of the heart.

Selective angiocardiography was then carried out by the injection of the contrast medium with a pressure apparatus through a catheter into the pulmonary artery. A very clear opacification of the somewhat dilated pulmonary vessels was obtained in this manner. At the same time as the contrast medium reached the left atrium via the pulmonary veins, filling of the persistent left superior vena cava was observed. This vein converged centrally with the left superior pulmonary vein, so that these vessels opened together into the left atrium. This chamber of the heart was otherwise unchanged. The contrast medium passed via the left superior vena cava peripherally to the left innominate vein and then through the right superior vena cava to the right atrium (Figs. 2 a and 2 b). The systemic veins that were filled with contrast medium and the right atrium

were clearly dilated. A large portion of the contrast medium passed in this way from the left atrium and left superior pulmonary vein into the left superior vena cava. These were the anomalous connections that formed the anatomic foundation for the left-to-right shunt.

Good opacification was observed almost simultaneously in both the left atrium and the left superior pulmonary vein as well as in the left superior vena cava. It was therefore impossible to determine definitely the extent to which the recirculating contrast medium proceeded from the left atrium and the left superior pulmonary vein respectively.

Discussion

The mediastinal contour in the frontal roentgenograms had a rather characteristic appearance. This was because both superior venae cavae bulged laterally. The same appearance, in point of principle, has been described by SNELLEN & ALBERS, inter alios, in patients in whom the principal part of the pulmonary veins drained into the left superior vena cava. However, no connection between this vein and the left atrium was demonstrated in these cases. Dilatation of the right superior vena cava and congestion of the pulmonary vessels must be interpreted as meaning that an extra large quantity of blood circulates via the former vein through the right heart out into the pulmonary circulation. The cause may be an abnormal connection between the right and left sides of the heart with recirculation of the pulmonary blood.

By right-heart catheterization with blood-gas analyses a return of pulmonary blood into the systemic veins was demonstrated. To a certain extent this investigation also afforded information concerning the site of the anomalous connection. On the other hand, no direct conception of the character of the actual anatomic changes was obtained. A proper application of angiocardiography was essential to the determination of the latter. In this case selective angiocardiography was chosen.

The principle upon which this procedure is based is a selective filling of the affected vessels and cavities of the heart, preferably through the direct injection of the contrast medium. In the case reported it was a question of opacifying the anomalous connection through which the arterialized blood was abnormally shunted. For this reason the contrast medium had to be concentrated in the pulmonary veins and the left atrium, so that the recirculation could be visualized as clearly as possible. Direct injection into the pulmonary veins or the left atrium is impossible. The contrast medium was therefore injected with pressure apparatus through a catheter into the pulmonary artery. Under these conditions this procedure could be expected to give the most rapid and clear opacification of the region in question.

By means of selective angiocardiography, visualization of the cavities of the heart and vessels not relevant to the problem under investigation

may also be avoided. Contrast medium within these may project over and possibly mask the actual changes.

In the case reported, the systemic veins in question and the right heart were visualized only by means of the recirculating contrast medium, through which the underlying anatomic cause of the left-to-right shunt became clearly evident. On the other hand, if the contrast medium had been injected intravenously, the vena cava system and the right heart would have been opacified before the contrast medium was abnormally returned. In addition, an intravenous injection into the left arm might cause a temporary rise in pressure within the systemic veins. This introduces the risk that the contrast medium may pass centrally through the left superior vena cava, although under ordinary pressure conditions the flow in this vein was peripherally due to the recirculating pulmonary blood. In earlier publications (cf. page 2) this source of error has not been considered. The intravenous injection of contrast medium from the left arm probably gives adequate information concerning circulatory conditions only in cases in which the blood flows in a central direction in the left superior vena cava.

In the investigation of patients with a left superior vena cava opening into the left atrium, with a left-to-right shunt, injection of the contrast medium into the pulmonary artery is therefore preferable to intravenous injection. The latter is indicated only if earlier methods of investigation have given incomplete information concerning the type and site of the changes. Under such circumstances, a general view of the intrathoracic circulation is necessary, and this may expediently be obtained by intravenous angiocardiography.

In the present case, it was possible with selective angiocardiography to obtain an unequivocal exposition of the anatomic malformations and their connection with the changed circulatory conditions. With this information as a point of departure the possibilities of surgical correction of the malformations may, with justification, be discussed. If right heart failure should occur, a ligation of the left superior vena cava may be considered and, in this manner, the abnormal return of pulmonary blood totally cut off.

SUMMARY

A case is reported of a persistent left superior vena cava communicating with the left atrium and left superior pulmonary vein. The roentgenologic appearances and indications for different angiocardiographic procedures are discussed.

ZUSAMMENFASSUNG

Ein Fall mit einer persistierenden Vena cava superior, die mit dem linken Vorhof und der linken Vena pulmonalis superior kommunizierte, wird beschrieben. Das rönt-

genologische Aussehen und die Indikationen für die verschiedenen angiographischen Prozeduren werden diskutiert.

RÉSUMÉ

Présentation d'un cas de veine cave supérieure gauche persistante communiquant avec l'oreillette gauche et la veine pulmonaire supérieure gauche. L'auteur discute les aspects radiographiques et les indications des différentes méthodes angiocardiographiques.

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THE ADNEXAL BRANCHES OF THE UTERINE ARTERY

An Arteriographic Study in Human Subjects

by

U. Borell and *I. Fernström*

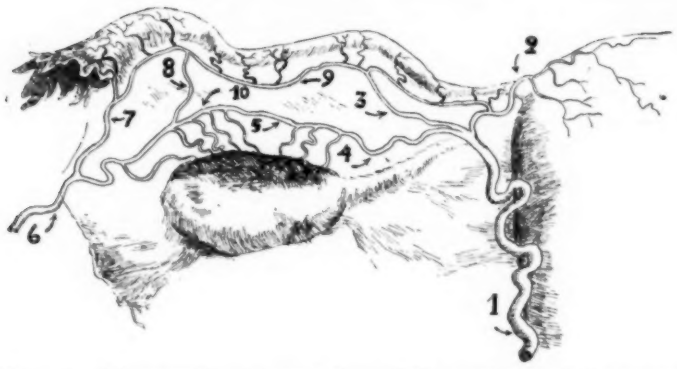
During the last two years we have examined more than 300 cases by pelvic arteriography. In a comparatively large number of arteriograms, the uterine artery was seen to send a branch to the adnexa. The present investigation was carried out to determine whether there is any difference between the radiographic appearance of the adnexal branches of the uterine artery in healthy and diseased adnexa. Such an investigation in human subjects has not previously been carried out, to the best of our knowledge. It was hoped that pelvic arteriography might provide a new approach to the differential diagnosis between salpingitis, tubal pregnancy and tumours of the ovary.

The Anatomy of the Adnexal Blood Vessels

The anatomy of the adnexal blood vessels has been studied in autopsy specimens by the injection or corrosion technique and by roentgen examination after the injection of an opaque substance into the uterine and ovarian artery (Luschka 1864; Hyrtl 1873; Broeckaert 1892; Davidsohn 1892—93; Souligoux 1894; Nagel 1897; Fredet 1899; Freund 1904; Redlich 1909; Laffont and Ezes 1929; Joachimovitz 1931; Léon and Raymond Dieulafé 1935; Massabuau et al. 1936; Solotuchin 1937; Mocquot et al. 1938; and others).

The blood supply of the tube and ovary is generally derived from both the uterine and ovarian artery. The anatomy and distribution of the adnexal blood vessels present great variation. According to a number of investigators the type of adnexal blood vessel shown in Diagr. 1 is most frequently encountered.

Submitted for publication, July 3, 1953.



Diagr. 1. Diagramatic representation of the anatomy of the adnexal branches. 1, uterine artery; 2, ramus recurrens; 3, ramus tubarii medialis; 4, ramus ovarii medialis; 5, ovarian arcade; 6, ovarian artery; 7, ramus infundibuli; 8, ramus tubarii lateralis; 9, tubal arcade; 10, ramus ovarii lateralis.

The uterine artery (1) divides into three branches just below the level of the uterine cornu. One of these, the ramus recurrens (2) runs first somewhat laterally and then bends upwards to run medially to the fundus uteri, partly supplying this portion of the uterus. Occasionally it is seen to send a twig to the extreme proximal portion of the tube. The second branch, the ramus tubarii medialis (3), runs to the tube, generally supplying its medial two-thirds. At times it may supply either the entire length of the tube or only a small part of it. The third branch, the ramus ovarii medialis (4), runs along the lower margin of the ligamentum ovarii proprium to the mesoovarium; it sends branches to the ovary and ends by anastomosing (5) with the ramus ovarii lateralis which arises from the ovarian artery.

The ovarian artery (6) generally arises from the aorta (GÉRARD 1913; HASSELHORST and SCHILLING 1926) and on reaching the true pelvis also divides into three branches. One branch, the ramus infundibuli (7) runs to the fimbriated end of the tube; the second branch, the ramus tubarii lateralis (8), supplies the lateral third of the tube in most cases. The ramus infundibuli anastomoses with the ramus tubarii lateralis which ends by anastomosing with the tubal branch of the uterine artery, the so-called tubal arcade being thereby formed and which runs parallel to the tube in the mesosalpinx. The ovarian artery continues as its third branch, the ramus ovarii lateralis (10), which supplies the lateral portion of the ovary and anastomoses with the ramus ovarii medialis of the uterine artery to form the ovarian arcade (5).

The general opinion is that the uterine artery supplies the medial half of the ovary and the medial two-thirds of the tube, the rest of their blood supply coming from the ovarian artery. The distribution of these arteries, however, shows great variation. In extreme cases either artery alone may supply the entire tube and ovary.

Determination of the distribution of blood vessels and of the direction of blood flow in autopsy specimens by an injection technique naturally present considerable difficulty. It appears that earlier investigators judged the direction of blood flow by the gradation of calibre of the blood vessels and the angle which their branches formed with them. It is, however, only by studies in vivo that further information may be obtained.

Material and Methods

The arteriograms of 326 cases were studied. One hundred and fifty-five were excluded for various reasons. One reason was that the quality of the films was poor. Another reason was that the examination had been terminated before opacification of the adnexal branches of the uterine artery had been obtained, or other blood vessels in the true pelvis were found to be projected over these arteries, making their identification impossible. Of the remaining 171 cases, the adnexal blood vessel was clearly visible in 69 (40 per cent). It should be mentioned, however, that good visualization of the uterine artery of one side only was obtained in the majority of these cases. For this reason, only the ipsolateral adnexal branch could be investigated.

Table 1

Cases Investigated

Diagnosis	Total No. of cases	Adnexal branch visible No. of cases	Adnexal branch not visible No. of cases
Control cases	18	11	7
Salpingitis	9	9	0
Tubal pregnancy	12	11	1
Tumours of the ovary	27	20	7
Myoma	62	7	55
Intra-uterine pregnancy	35	5	30
Amenorrhoea (prior to hormone therapy).	8	6	2
Total No. of cases	171	69	102

Table 1 shows the type of case studied together with the number of cases both in which an adnexal branch was visible and in which it did not show up.

All patients in this series with amenorrhoea were treated with hormones. Each patient was given a course of intramuscular injections of oestradiol monobenzoate in doses of 50,000 IbU daily for six consecutive days followed by a course of intramuscular injections of progesterone in doses of 100 mg daily, divided into two injections of 50 mg each for the next six days. On the third day of the progesterone treatment, each patient was also given 10,000 IbU of oestradiol monobenzoate intramuscularly. The radiologic investigation was made on three occasions in each case of this group: The first before endocrine therapy was begun, the second after administration of oestradiol monobenzoate, and the third after the progesterone course.

In the majority of the cases of this series pelvic arteriography was carried out by the method devised in the Roentgen Department of Karolinska Sjukhuset and described in a previous paper (BORELL et al. 1952), taking three films at intervals of two or three seconds in each case. In a number of cases we have also used the technique described by SELDINGER (1953).

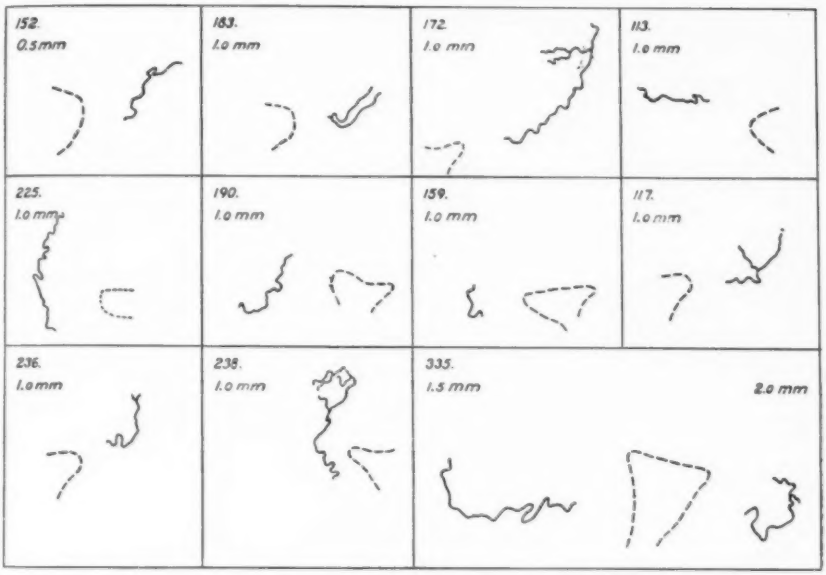
As a rule, the adnexal branch of the uterine artery did not show up in the first film but was clearly visible in the second and third. The other blood vessels in the true pelvis were then generally no longer opacified.

The width of the uterine artery and its adnexal branch was measured directly from the arteriograms to an accuracy of 0.5 mm. The measurements of the uterine artery were made at the point where it leaves the lateral pelvic wall. The width of the adnexal branch was measured at its point of origin. We also investigated the course of the adnexal blood vessel. A drawing of its course was reproduced on tracing paper directly from the films in each case in which it was visible. The tracings, which do not show the variations in the width of the vessel, are compiled in Diagr. 2, 3, 4, 5 a and b, 6, 7. The width of the blood vessel is given in mm.

In view of the fact that it was not possible in most cases to determine whether the branch seen was the ramus tubarii medialis or the ramus ovarii medialis the term 'ramus' throughout this paper denotes the adnexal branch of the uterine artery.

Results

A. *Control cases* (Diagr. 2, Figs. 1, 2). This group included 18 cases. Bimanual examination revealed no pelvic abnormality in any of them. A ramus showed up in 11 cases, being clearly visible on both sides in 1. In 7 cases it could not be identified. In the 11 cases where a ramus was identified, the patient was of reproductive age and had a normal men-



Diagr. 2. The appearance of the ramus in cases of normal adnexa. Record number of the arteriogram in the upper left corner. Width of the ramus in mm. Broken line indicates the corpus uteri.

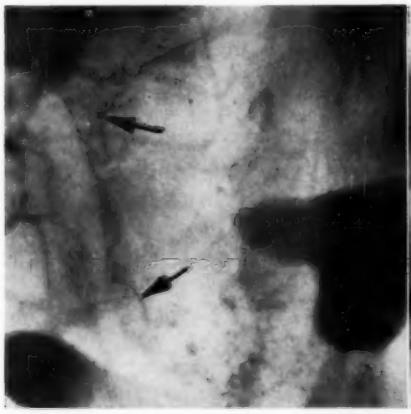


Fig. 1. (P. ang. 225.) Arteriogram and hysterogram of a case of primary infertility. Ramus indicated by arrows.

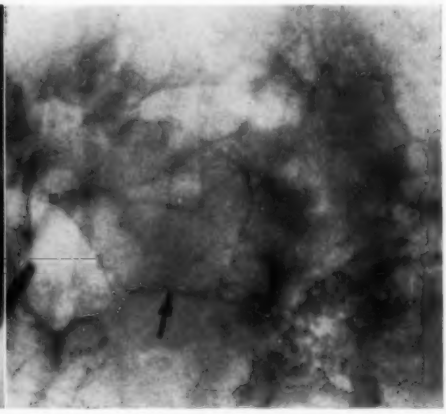
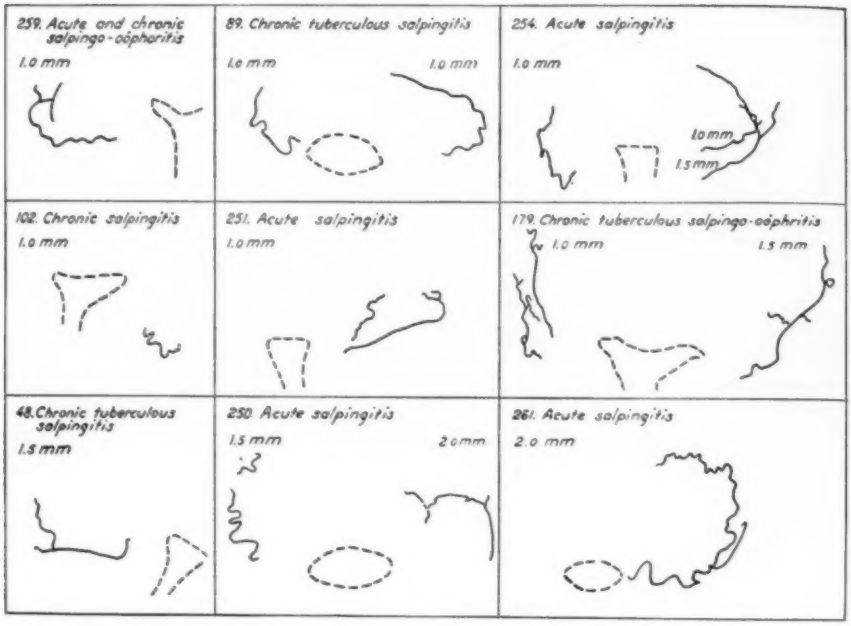


Fig. 2. (P. ang. 113.) Arteriogram of a case of secondary infertility. Arrow indicates ramus.



Diagr. 3. The appearance of the ramus in cases of salpingitis.

strual history in 10, and in 1 case the menopause had occurred three years previously. (P. ang. (= pelvic arteriography) No. 172).

Width of the ramus. Of the 12 rami investigated, 9 measured 1.0 mm in width. This figure closely approximated its average width in this group which was 1.1 mm. It was found that there was no constant difference in width between the rami in an upright and an anteflexed uterus. It may therefore reasonably be assumed that the slight variation in radiographic magnification caused by variation in the position of the uterus did not have any noteworthy influence on the measurements as these were made to an accuracy of only 0.5 mm.

Course of the ramus. The ramus was generally seen to follow a tortuous course. Its length varied. Eight of the 12 rami investigated were found to be short whilst the other 4 were much longer, probably because they supplied a greater portion of the adnexa.

Evidence of branching of the ramus. In 7 cases the ramus was not seen to give off any branches. Of the remaining cases, 1 branch was identified in 3, 2 branches in 1, and 3 branches in 1 case.

Fig. 3. (P. ang. 261.) Arteriogram in a case of acute salpingitis. Arrows indicate ramus.

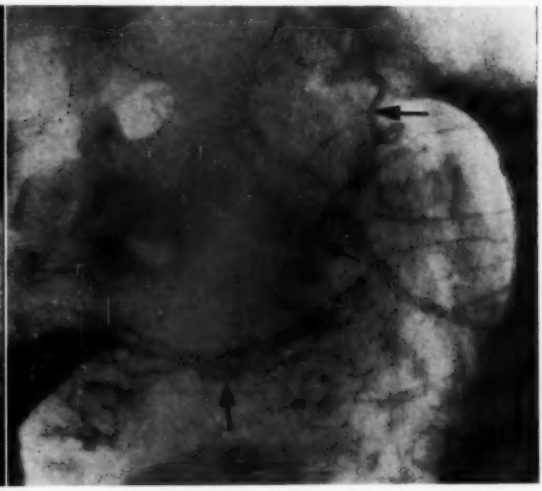


Fig. 4. (P. ang. 179.) Arteriogram and hysterogram in a case of chronic tuberculous salpingo-oophoritis.

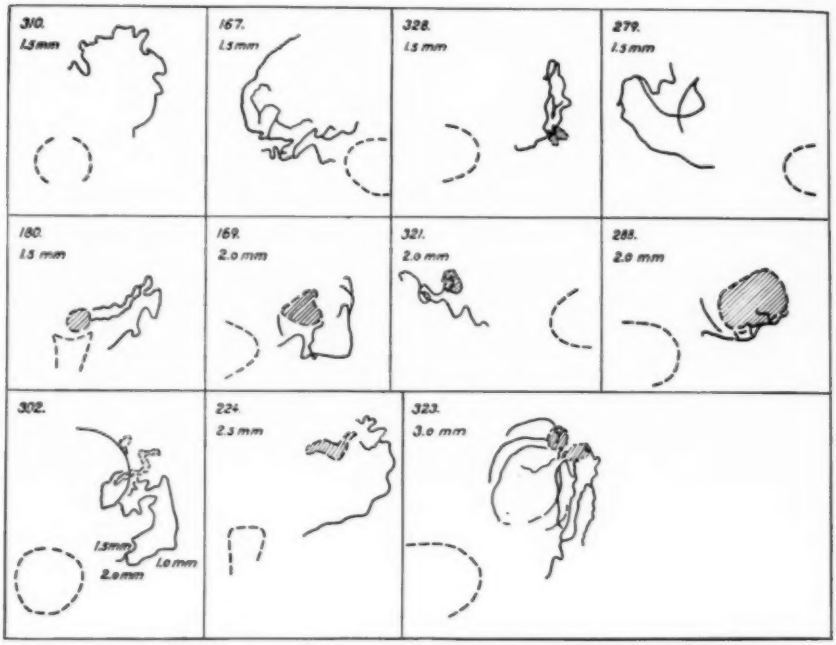
B. *Cases of salpingitis* (Diagr. 3, Figs. 3, 4). This group included 9 patients; 5 of them had chronic and 4 acute salpingitis. In one of the former there was a history of a recent flare-up of the disease. A ramus was visible in all these cases.

Width of the ramus. The ramus was found to be slightly wider than in the controls, particularly in the cases of acute salpingitis, its average width being 1.3 mm. In 2 cases of acute salpingitis, the ramus was slightly wider even than the uterine artery. In the other cases, there was a difference in width between the two arteries of up to 1.5 mm.

Course of the ramus. The ramus was found to follow a slightly straighter course than in the control cases. This was probably due to thickening of the tubal wall. There was no radiographic evidence to indicate that the degree of tubal thickening bore any relation to the degree of straightening of the ramus. In most cases the ramus was found to be longer than in the control group.

Evidence of branching of the ramus. Eight of 13 rami studied divided into branches. These were few in number, the maximum present being 3. The number of cases, in which branches of the ramus were visible, was practically the same in cases of acute and chronic salpingitis.

C. *Cases of tubal pregnancy* (Diagr. 4, Figs. 5, 6). This group included 12 cases. In one of them there was no radiographic evidence either of the



Diagr. 4. The appearance of the ramus in tubal pregnancy. The shaded areas indicate opacified placental sinuses.

uterine artery or of a ramus. In the 11 cases in which a ramus was visible, the duration of pregnancy varied between 5 and 13 weeks. In 6 of these cases the site of attachment of the placenta was in the ampullary third, and in 5 in the middle third of the tube. Placental sinuses were visible in 3 of the former and in all cases of the latter group.

Width of the ramus. The average width of the ramus was 1.9 mm in this group. The ramus was found to be widest in the most advanced pregnancies. In 6 cases, there was no difference in width between the uterine artery and the ramus. In 2 cases, the ramus was found to be wider than the uterine artery and in 2 cases, the reverse was noted.

Course of the ramus. The ramus was generally seen to follow a less tortuous course and to be longer than in the control cases.

Evidence of branching of the ramus. With one exception, the ramus was seen to divide into several branches in all cases of this group. In 1 case, no less than 9 branches were visible. In 5 cases, the appearance of certain branches was found to be very characteristic: They were straight-

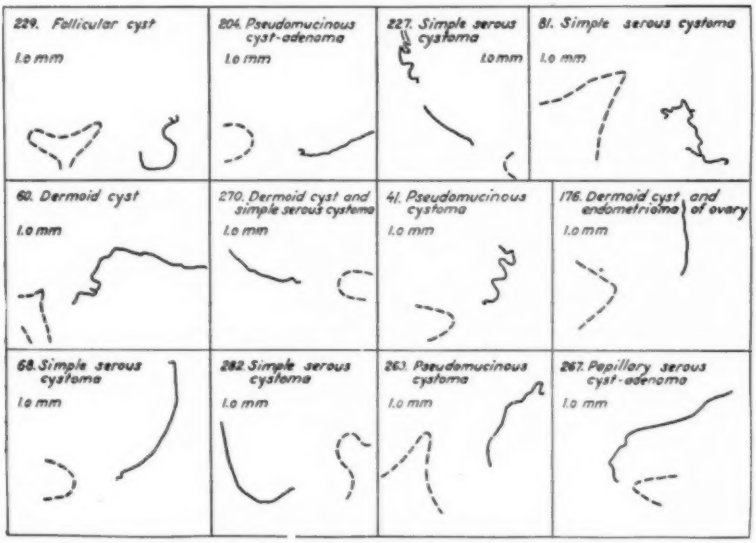
Fig. 5. (P. ang. 302.) Arteriogram in a case of tubal pregnancy. Two rami (arrows a and b) may be seen running to the tube. The unmarked arrow indicates a typically stretched-out and arched blood vessel. Arrow c indicates opacified placental sinuses.

Fig. 6. (P. ang. 323.) Arteriogram in a case of tubal pregnancy. Arrow a points to the ramus. The unmarked arrow indicates a typically stretched-out and arched blood vessel. Arrow b indicates placental sinuses beginning to show up.

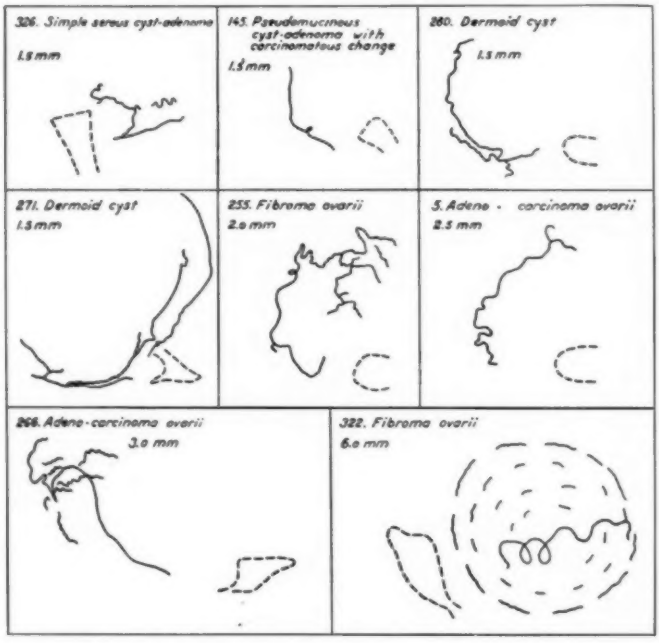
ened-out, arched, and were seen running in the thickened tubal wall (p. ang. Nos. 279, 169, 288, 302, 323). It is interesting to note that it was only in the cases of tubal pregnancy and in one case of chronic salpingitis that this type of branch of the ramus was seen.

D. *Cases of tumours of the ovary* (Diagr. 5 a, b, Figs. 7, 8, 9, 10 a, 10 b, 11 a, 11 b). Of the 27 cases of this group, a ramus was clearly visible in 20. The type and size of the tumours varied. In 7 cases, including 1 case of ovarian fibroma, 1 case of ovarian cyst with torsion of the pedicle, 3 cases of simple ovarian cysts, and 1 case of carcinoma of the ovary, there was no radiographic evidence of a ramus.

Width of the ramus. It is interesting to note that the ramus was found to be markedly widened in the cases of fibroma and carcinoma of the ovary, measuring between 2.0 and 6.0 mm in width. In the other cases, its width varied between 1.0 and 1.5 mm. The average width of the ramus for the whole group was 1.5 mm. The difference in width between



a.



b.

Diagr. 5 a and b. The appearance of the ramus in cases of ovarian tumours.

Fig. 7. (P. ang. 68.) Arteriogram in a case of simple cyst of the ovary. The arrow points to the ramus which is straightened-out.

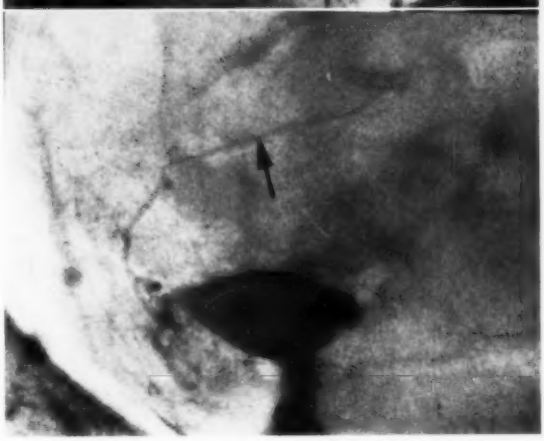


Fig. 8. (P. ang. 267.) Arteriogram and hysterogram in a case of papillary serous cystadenoma. The arrow points to the straightened-out ramus.

the uterine artery and the ramus generally varied between 0.5 and 1.5 mm. In the cases in which the ramus was markedly widened it was either as wide as, or wider than the uterine artery.

Course of the ramus. The ramus was seen to follow a straight course in all but 4 cases of this group. There was no radiographic evidence that the size of the tumour bore any relation to the degree of straightening of the blood vessel. There appeared to be a correlation between the length and width of the ramus because it was found to be longest in the cases in which it was widest.

Evidence of branching of the ramus. Of the 20 cases in which a ramus was visible it was seen to divide into branches in 8. Especially in the cases in which the ramus was wide were several branches visible, the

Fig. 9. (P. ang. 255.) Arteriogram in a case of fibroma of the ovary. The arrows point to the ramus.

largest number being seen in the cases of fibroma and carcinoma of the ovary.

E. *Cases of myoma* (Diagr. 6). This group included 62 cases. A ramus was visible in 7 cases only. The size of the myoma varied between the size of a hazel-nut and that of a croquet-ball. There was no radiographic evidence that visualization of a ramus bore any relation to the size of the tumour.

The width of the ramus. The width of the ramus in this group was practically identical with that of the ramus in the control group, the average width being 0.9 mm. In most cases the difference in width between the uterine artery and the ramus was found to be greater than in the control group. The explanation lies in the fact that the uterine artery in cases of myoma is wider than in normal cases.

Course of the ramus. The ramus was seen to follow a tortuous course identical with that noted in the control cases. In one case it was straighter (p. ang. No. 210). This was probably due to enlargement of the adnexa caused by the tumour.

Evidence of branching of the ramus. The ramus was not seen to divide into branches in any of these cases.

F. *Cases of amenorrhoea.* (Diagr. 7, Figs. 12a, 12b, 12c). This group included 8 patients. A ramus was seen in 6 of them before hormone

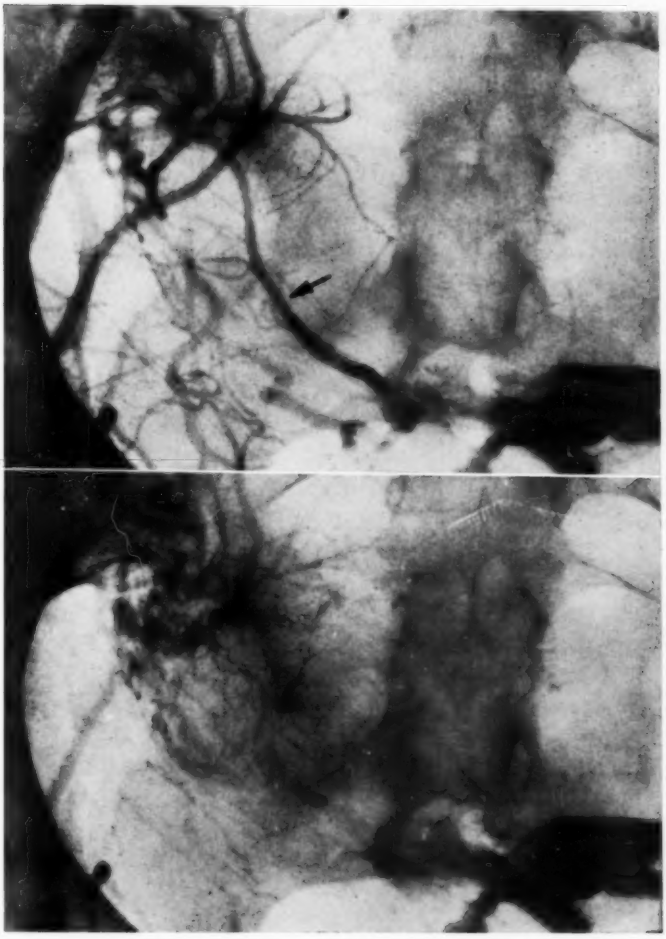
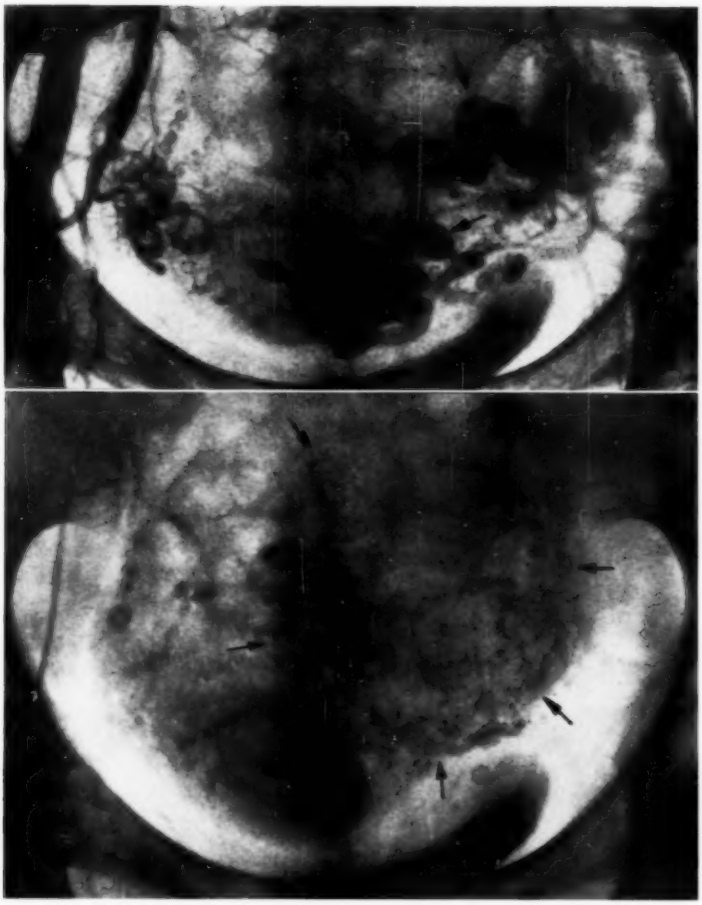


Fig. 10. (P. ang. 266.) a. Arteriogram and hysterogram in a case of adenocarcinoma of the ovary. The arrow points to the widened and straightened-out ramus.

b. Film taken about 2 seconds after film 10 a. On the left in the true pelvis at the site of the tumour, numerous small opacified blood vessels may be seen.

therapy. After hormone therapy, it was impossible to measure the width in three cases, in which the quality of the films was poor.

Width of the ramus. The average width of the ramus was found to be 0.6 mm. This value was lower than that obtained in the control cases.



a.

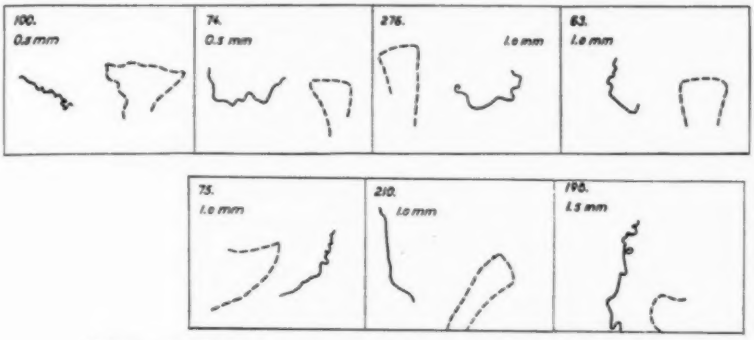
b.

Fig. 11. (P. ang. 322.) a. Arteriogram and unsuccessful hysterogram showing vaginal reflux of opaque medium. The arrow points to the ramus which is markedly widened.

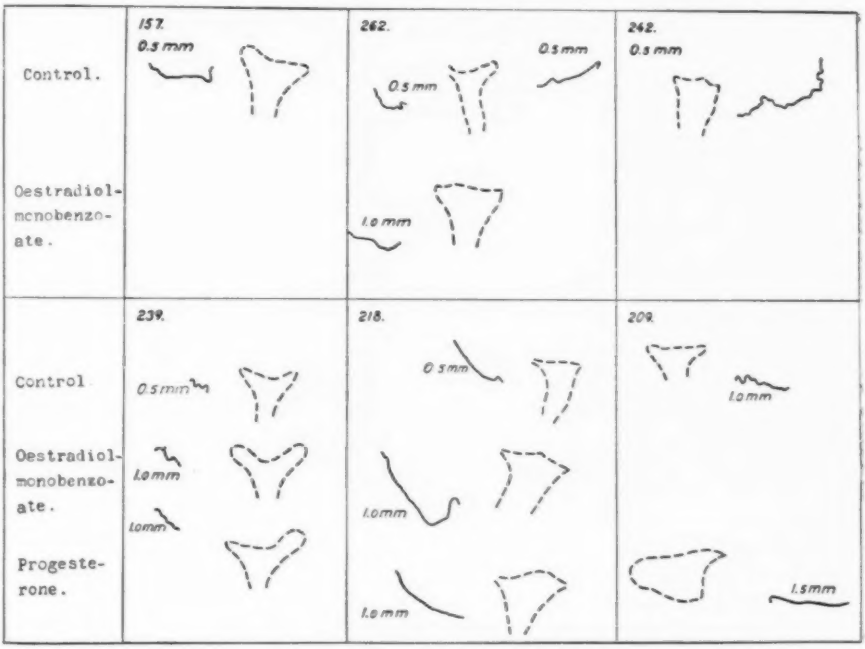
b. Film taken about 2 seconds later. The arrows surround the ovarian tumour which shows up as the result of filling of numerous blood vessels.

An increase in width was noted after a course of intramuscular injections of oestradiol monobenzoate. The increase was 0.5 mm. Subsequent progesterone therapy did not cause any further change.

The course of the ramus. The ramus was found to follow practically the same course as in the control group before the patients were submitted

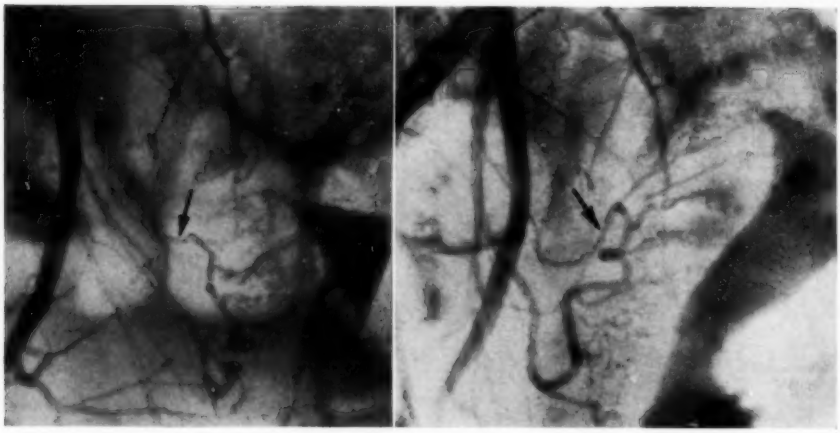


Diagr. 6. The appearance of the ramus in cases of myoma.



Diagr. 7. The appearance of the ramus preceding and following hormone therapy in cases of amenorrhoea.

to hormone therapy. In one case of primary amenorrhoea, however, it was seen to be quite straight prior to, as well as after hormone therapy (p. ang. No. 218). Hormone therapy did not cause any change in the pattern of its course.



a. b.

c.

Fig. 12. (P. ang. 218.) Arteriogram and hysterogram in cases of primary amenorrhoea. The arrow indicates the ramus.

a, prior to treatment.

b, after treatment with oestradiol monobenzoate.

c, after treatment with progesterone.

Evidence of branching of the ramus. The ramus was not seen to divide into branches in any of the cases of this group.

G. *Cases of intra-uterine pregnancy.* This group included 35 cases. The duration of pregnancy varied. A ramus was visible in 5 cases only, and it is interesting to note that in all these cases the pregnancy was at a very early stage, *i. e.* 8 weeks or under.

Width and course of the ramus. The ramus corresponded to that in the control group in respect to width and course. It was therefore deemed unnecessary to tabulate the measurements and to append tracings of its course.

Evidence of branching of the ramus. In none of the cases of this group was the ramus seen to branch.

Discussion

In this investigation of the uterine artery by pelvic arteriography a branch to the adnexa was seen in a large number of cases; it was possible to investigate its width, course, and distribution. It was found that these anatomic features of the blood vessel showed more or less constant changes in certain cases of adnexal lesions.

In some cases of salpingitis it was apparent that the adnexal branch of the uterine artery was longer and followed a less tortuous course than in the control cases. The obliteration of tortuosity is probably due to thickening of the tubal wall. Otherwise, its appearance did not deviate from that of the ramus in the control cases. It is therefore difficult to differentiate the arteriogram of a woman with salpingitis from the arteriogram of a healthy woman.

In the cases of tumours of the ovary, the adnexal branch of the uterine artery followed a much straighter course than in the control cases, being even straighter than in some cases of salpingitis. The cause of the straightening of the blood vessel is probably to be found in the expansion of the adnexa caused by the ovarian tumour. It is interesting to note that in the cases of carcinoma and fibroma of the ovary it supplied a very large portion of the adnexa and the opaque medium passed from it into tumour tissue. Moreover, in these cases it was much wider than in the other cases of this group. It should be mentioned, however, that these changes in the adnexal branch of the uterine artery were not a constant finding. Among the cases of tumours of the ovary in which the adnexal branch was not visible, were two cases of carcinoma and one case of fibroma of the ovary. The explanation of its absence probably is that the blood supply of the tumour in some cases is derived from the ovarian artery whilst in others it comes from the uterine artery. The possibility of carcinoma or fibroma, therefore, cannot be ruled out in cases of tumour of the ovary, in which the adnexal branch of the uterine artery is not visible in the arteriogram.

In tubal pregnancy the changes in the adnexal blood vessel were found to be so characteristic that the correct diagnosis could be established from the arteriogram in the majority of cases. If there is radiographic evidence of a wide adnexal blood vessel following a fairly straight course and dividing into branches some of which are stretched out and arched, tubal pregnancy is strongly suggested. If placental sinuses are also visible, this is proof-positive of the presence of a tubal pregnancy (Borell et al. 1953). Tubal pregnancy may be difficult to differentiate from carcinoma or fibroma of the ovary because the adnexal blood vessel may divide into many branches also in these cases. However, if its branches are seen to be

stretched out and arched, and placental sinuses are apparent, the differential diagnosis presents no difficulty.

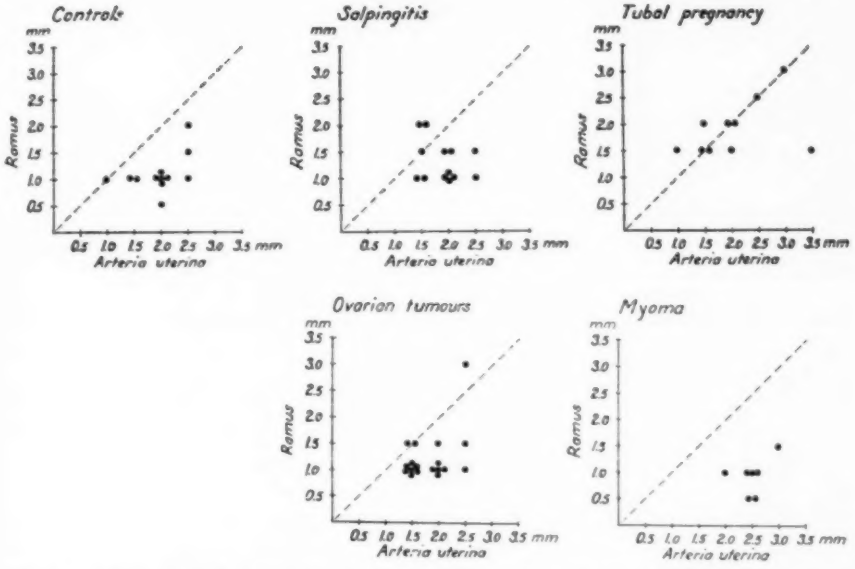
The radiographic appearance of the adnexal branch of the uterine artery in cases of myoma did not deviate from that in the control cases. As already mentioned, it was visible only in a few cases of this group. Two explanations of its absence in the other cases are possible: Firstly, that the appearance of the uterine artery and its branches was so changed that it was impossible to identify the adnexal vessel; secondly, that the ovarian artery becomes enlarged and participates in supplying the myomatous uterus, the blood in the adnexa flowing in the direction of, and into the corpus uteri.

Similarly, in the cases of intra-uterine pregnancy, the radiographic appearance of the adnexal branch of the uterine artery corresponded to that in the control cases. The explanation of the paucity of the cases in which it was visible, probably is that blood in this artery flows in the direction of the corpus uteri. According to a number of investigators (LUSCHKA 1864, BROEKAERT 1892, and others) the ovarian artery supplies a portion of the corpus during pregnancy.

In the controls, cases of salpingitis, tubal pregnancy, tumours of the ovary, and cases of amenorrhoea, an adnexal branch of the uterine artery was visible in 57 whilst in 17 cases it was not seen. This suggests that the blood supply of the adnexa is derived from the uterine artery in many cases.

It is interesting to note that in most cases the uterine artery was seen to give off only one ramus to the adnexa. This is not in line with the observations made in autopsy specimens investigated by injection technique where the uterine artery was generally seen to divide into two branches, one running to the tube and the other to the ovary. In some of the 69 cases of this series in which visualization of both uterine arteries was obtained, they were sufficiently well filled to define the adnexal branches on both sides. We had thus altogether 82 branches available for investigation. In only 7 cases was the uterine artery seen to divide into two branches — probably the ramus tubarii medialis and ramus ovarii medialis. Two explanations of the absence of the second branch in the other cases are possible: Firstly, that it was too small to opacify; secondly, that the second vessel originated from the ovarian and not from the uterine artery.

Only in the cases in which a blood vessel was visible within the adnexal tumour was it possible to determine which branch of the uterine artery it represented. In 8 cases of tubal pregnancy, the opaque medium passed into placental sinuses via an adnexal branch of the uterine artery. This was evidence that the branch seen was the ramus tubarii medialis. In 5 cases of ovarian tumour, the blood supply of the tumour was derived from



Diagr. 8. Correlation between the width of the uterine artery and that of the ramus in the controls, cases of salpingitis, tubal pregnancy, tumours of the ovary and myoma. The broken line indicates that their width is identical.

the uterine artery via an adnexal branch. In these cases the branch seen was unquestionably the ramus ovarii medialis.

The present investigation in vivo gives further support to the views expressed by earlier workers that the source of the arterial blood supply of the adnexa, and the distribution of the branches of the ovarian and uterine arteries in these organs show great variation. All possibilities may occur, ranging from cases in which the ovarian artery supplies the entire tube and ovary to cases in which the blood supply of these organs is solely derived from the uterine artery. Evidence in support of the view that the uterine artery may supply the entire length of the tube, or practically its entire length, was found in cases of tubal pregnancy situated in the ampullary end of the tube. In these, the opaque medium passed into the placental sinuses through the adnexal branch of the uterine artery (p. ang. Nos. 328, 180, 169). The case of fibroma of the ovary in which the entire tumour was outlined as a result of filling of numerous small blood vessels via a ramus ovarii medialis demonstrated that the uterine artery may supply the entire ovary (Figs. 11 a and 11 b). Normal ovarian tissue was not found at operation, the tumour having supplanted

the ovary. On the other hand, both uterine arteries were absent in one case of tubal pregnancy of this series. This case suggested that the ovarian artery alone may supply the entire tube and ovary (p. ang. No. 172). It is therefore necessary to fill the ovarian artery in cases of adnexal tumours, in which it is not possible to obtain filling of the adnexal branch via the uterine artery. For this reason we now also fill the ovarian artery by aortography in such cases. This is an easy procedure if Seldinger's catheter is used.

In a previous paper it was shown that the width of the uterine artery increases under the influence of ovarian hormones whilst the width of the other vessels in the true pelvis remained unchanged (BORELL et al. 1953). In the present investigation it was found that the width of its adnexal branch or branches also increased after hormone therapy.

On comparing the width of the uterine artery with that of its adnexal branch, it was found that they were practically identical in the cases of tubal pregnancy whilst in the control cases and in the majority of the cases of salpingitis and ovarian tumour the uterine artery was wider than its adnexal branch (Diagr. 8). In the cases of myoma, the uterine artery was generally found to be markedly wider than in the control cases whilst the width of its adnexal branch was practically the same in both groups.

SUMMARY

Of 171 cases examined by pelvic arteriography the uterine artery was seen to send a branch to the adnexa in 69. The width, course, and the branching of the adnexal artery was investigated in cases of salpingitis, tumours of the ovary, tubal pregnancy, amenorrhoea and in normal intra-uterine pregnancy, using cases of normal adnexa as controls. The artery was found to present such characteristic changes in many cases of ovarian tumour and tubal pregnancy that their arteriographic appearances were diagnostic. The width of the artery was found to increase after treatment with ovarian hormones in cases of amenorrhoea.

The present in vivo investigation confirmed the observations made by earlier investigators on autopsy specimens investigated by the injection technique that the distribution of the uterine and ovarian arteries in the adnexa shows great variation.

ZUSAMMENFASSUNG

Bei 171 mit Beckenarteriographie untersuchten Fällen fand man, dass die A. uterina in 69 Fällen einen Ast zu den Adnexen schickte. Die Lumenweite, der Verlauf und die Verzweigung der Adnexarterie wurde bei Salpingitis, Ovarialtumoren, Tubenschwangerschaft, Amenorrhöe und bei normalen intrauterinen Schwangerschaften untersucht und mit Fällen mit normalen Adnexen verglichen. Man fand, dass die Arterie in vielen Fällen von Ovarialtumoren und Tubenschwangerschaften so charakteristische Veränderungen zeigt, dass ihr arteriographisches Aussehen die Stellung der Diagnose ermöglichte. Man fand auch, dass die Weite der Arterie nach Behandlung von Amenorrhöe mit Ovarialhormonen zunahm.

Die vorliegende Untersuchung in vivo bestätigt die Beobachtungen, welche von früheren Untersuchern an Leichenpräparaten mit Hilfe der Injektionstechnik angestellt worden sind, nämlich dass der Verlauf der A. uterina und der A. ovarica in den Adnexen sehr verschiedenartig ist.

RÉSUMÉ

Sur 171 cas d'artériographie pelvienne, on a vu l'artère utérine envoyer une branche aux annexes dans 69 cas. Le calibre, le trajet et la ramification de l'artère annexielle ont été étudiés dans des cas de salpingite, de tumeur de l'ovaire, de grossesse tubaire, d'aménorrhé et de grossesse intra-utérine normale, des cas d'annexes normales servant de témoins. Cette artère a présenté dans de nombreux cas de tumeur de l'ovaire et de grossesse tubaire des modifications si caractéristiques que leurs aspects artériographiques avaient une signification diagnostique. Dans des cas d'aménorrhée, le traitement par des hormones ovariennes a augmenté le calibre de l'artère.

Ces recherches in vivo ont confirmé les observations, faites par d'autres chercheurs sur des pièces d'autopsie par des techniques d'injection, concernant la grande variabilité de la distribution des artères ovarienne et utérine dans les annexes.

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STUDIES ON CONTRAST FILLING OF THE NORMAL APPENDIX

by

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The introduction of contrast media as diagnostic agents in diseases of the gastro-intestinal tract opened a new wide field of roentgen examinations. In view of the difficulties which may be involved in the clinical diagnosis of appendicitis, especially the chronic variety, it was but natural that efforts were made to extend these examinations to the appendix.

In 1909, BÉCLÈRE reported a case in which he had obtained filling of the appendix with a bismuth suspension. Since then, a large number of reports on this subject has been published.

Attempts have been made quite naturally to ascertain the frequency of contrast filling of the normal appendix; after oral administration of the contrast medium, which is by far the most common method, filling has been reported to occur in from 40 % to slightly less than 90 % of the cases studied.

More recently, CARSTENS (1949) found that the appendix failed to fill in twenty-five of a series of ninety healthy medical students. Barium was given by the oral route twice with an interval of ten hours between each administration. Fluoroscopic examinations were carried out at eight hours after the ingestion of the second contrast meal, at twenty-four hours, and then once daily during the next few days. The experiment was repeated on the twenty-five subjects who had not shown filling on the first occasion; filling was then observed in twelve additional cases, thus producing a total frequency of 85.5 per cent.

In his experiments, CARSTENS used barium sulphate only. Some investigators have used small fractionated doses of barium sulphate while others recommend the simultaneous administration of a saline laxative,

Submitted for publication, June 16, 1953.

resulting in a more liquid state of the intestinal contents during their passage into the cecum and thus facilitating influx into the appendix.

BUTLER (1950) reported that the addition of sodium carboxylmethyl cellulose (CMC) to the barium sulphate suspension resulted in a higher frequency of filling of the normal appendix but, unfortunately, did not specify the amounts and dosage used. FOUBERT and ROBERT (1951) used the same substance as a vehicle for the suspension in roentgenographic studies of the esophagus and stomach.

Methods and Material

CMC is made of pure cellulose and is used chemically in a water-soluble form. A solution of CMC is highly viscous, although its viscosity depends on the temperature. When CMC is placed in water, it at once forms clumps with a sticky, jelly-like outer layer, the central cores being quite dry. Water gradually diffuses into the centres, a process which may be greatly accelerated by increasing the temperature and/or by stirring. Animal experiments have shown that the substance is harmless, but it seems to be affected by intestinal enzymes, which are reported to bring about a certain disintegration evidenced, inter alia, by a decrease in the viscosity of aqueous CMC solutions.

In the experiments now reported, two CMC preparations, Cellugel f. f. 500 and Cellugel Super 15,000, were used, both of considerable viscosity (300—500 and 10,000 c. P., respectively, determined by the method of HØPPLER).

The experimental procedure used was the same in the series of experiments. A heaped tablespoonful of CMC was added to a glass of barium sulphate suspension. After vigorous stirring, the clumpy liquid was ingested, together with soda-water or beer, by the subject on a fasting stomach.

As far as it was possible to trace, the subjects examined in the three groups of experiments had never had any abdominal attacks suggestive of appendicitis. The largest group consisted of 21 female and 43 male patients admitted to the medical and surgical departments of the hospital for treatment of diseases not involving the gastro-intestinal tract — fractures, diabetes, asthma, eczema, etc. Men were preferred as subjects, because one can never be quite certain that a female patient may not, at some time, have suffered from diseases of the internal genitalia, which may give rise to periappendiceal adhesions and which, in turn, may impede the passage of the contrast medium into the appendix.

Of the 64 subjects, 42 received Cellugel Super 15,000, while 22 were given Cellugel f. f. 500.

As far as possible, the roentgen examinations were carried out within

the 3rd, 6th—7th, and 10th—11th hours after the ingestion of the contrast meal. On each fluoroscopic examination, an 18 × 24 cm film of the cecal region, including the ileocecal valve and the fundus of the cecum, and a 13 × 18 cm film of the distal portion of the cecum, under compression, were taken.

The degree of filling of the appendix was divided into three categories, filling at the base being indicated by +, partial and markedly segmented filling by ++ (fig. 5, 6), and filling to the tip by +++ (fig. 1—4).

During the fluoroscopic examination it was noted whether the appendix seemed to be freely movable or fixed, and its position was also studied.

It would have been of great interest to have studied the emptying of the appendix, since, in the literature, appendicostasis plays a great rôle as a criterion in the diagnosis of chronic appendicitis although it has not been agreed where the upper limit to the normal emptying time of the appendix should be set. However, we experienced the difficulty that it was often impossible to allow the patients to stay in hospital for a sufficiently long time for this examination, and the emptying of the appendix was not followed in all cases.

Table 1 shows the sex and age distribution of the 42 patients who received Cellugel Super 15,000.

Table 1

Sex and age distribution of the 42 patients who received Cellugel Super 15,000

Sex		Age, in years							
M.	F.	0—10	11—20	21—30	31—40	41—50	51—60	61—70	71—80
31	11.....	4	7	12	8	7	1	1	2

In these patients, filling of the appendix was seen in 40, whereas filling did not occur in a 19-year-old man and a 44-year-old woman.

One week later, the man was subjected to a renewed examination when a ++ filling was observed; the examination of the woman could not be repeated.

In 33 instances, the appendix filled to the tip (+++); in 6, the appendix showed scattered, segmented filling without a visible apical portion (++), and in 2, revealed filling only at the base (+).

Table 2

Degree of filling and number of cases showing mobility or medial position of the appendix in the 42 subjects who received Cellugel Super 15,000

Degree of filling			Mobility	Medial position
+++	++	+		
33	6	2	29	18

The most common appearance was that of a spotted, segmented filling of the appendix, in which the intestinal contents gave rise to zones of lessened density of varying size, but massive filling was not at all rare.

Mobility was demonstrated in 29 cases. In 18 patients, the appendix was seen distinctly medial to the cecum, with the tip pointing towards the midline.

It is of great practical importance to clarify how rapidly, filling of the appendix with contrast medium may be expected. For the understanding of the mechanism of filling a brief account of the anatomy and physiology of the normal appendix is necessary.

The normal appendix has an inner circular and an outer longitudinal layer of non-striated muscular fibers, with the most well-developed musculature in the proximal third. It has been observed that pilocarpine may induce shortening of the appendix, especially of the proximal third, the lumen of which is simultaneously contracted, so that the appendiceal contents are emptied. Conversely, atropin induces a relaxation of the tonus of the appendix with a resultant increase in the diameter of the lumen, with the greatest changes of form again in the proximal third.

Under normal conditions, filling of the appendix is passive and absolutely dependent on the movements of, and the pressure in, the cecum.

As early as three hours after the ingestion of the contrast meal the patients were subjected to fluoroscopic examination; the contrast medium was invariably found in the terminal loops of the ileum and in the cecum; however, even though favorable conditions for the filling of the appendix seemed to be present, this was seen only on five occasions. The times at which filling was observed in the 41 subjects are shown in table 3.

Table 3

Times at which filling was observed in the 41 subjects who received Cellugel Super 15,000. Within 7 hours filling had occurred in 32 cases

Hours after ingestion of contrast meal	3	4	4½	5	5½	6	6½	7	8½	10	22	23	24	48
No. of cases	5	2	1	3	3	6	5	7	1	2	2	1	2	1

From the table, it appears that in 32 of the 41 subjects the appendix had filled 7 hours after the administration of the contrast medium.

As already pointed out, we were unable to study the emptying in all cases, but in 17 instances it was found that the appendix had emptied after the lapse of 4 days.

Of the patients referred to us from the two aforementioned departments, 22 were given Cellugel f. f. 500, which has a much lower viscosity.

The sex and age distribution of these subjects appears from table 4.

Table 4

Sex and age distribution of the 22 subjects who received Cellugel f. f. 500

Sex			Age, in years					
M.	F.		0—10	11—20	21—30	31—40	41—50	51—60
12	10	.....	2	8	5	4	2	1

In this group of experiments, the appendix failed to fill in 3 instances: in a woman aged 21 and in two men, aged 21 and 27 years.

The experiment was repeated in the woman, and a ++ filling was then observed.

Complete filling was obtained in 15, partial spotted filling in 2, and filling at the base in 3 instances (table 5). Thus, filling was observed in 90.9 per cent of the cases. Table 6 shows the times at which filling was observed.

Table 5

Degree of filling and number of cases showing mobility or medial or lateral position of the appendix in the 22 subjects who received Cellugel f. f. 500

Degree of filling			Mobility	Medial position	Lateral position
+++	++	+			
15	2	3	11	10	3

Table 6

Times at which filling was observed in the 22 subjects who received Cellugel f. f. 500. Within 7 hours filling had occurred in 13 cases

Hours after ingestion of contrast meal	3	3½	4	5½	6	7	10½	11	13½
No. of cases	1	1	1	1	1	8	4	2	1

It appears that in two-thirds of the cases the appendix had filled within 7 hours after the ingestion of the contrast meal. In eleven of the subjects the appendix was distinctly mobile. In 10 cases the appendix was directed medially, while a definite lateral position with fixation was observed in 3 cases.

Before we proceed to the second group of investigations, the experimental results obtained in the first, will be summarized.

The subjects studied were patients from the medical and surgical departments with diseases not involving the gastro-intestinal tract and, as far as it was possible to ascertain, without a past history of appendicitis. To an ordinary barium sulphate contrast medium was added either Cellugel f. f. 500 or Cellugel Super 15,000, both carboxylmethyl cellulose preparations with a high viscosity.

Cellugel Super 15,000, having a higher viscosity, gave filling of the appendix in 97.6 % of the cases, and in 80 % filling occurred within 7 hours after the ingestion of the contrast meal.

Cellugel f. f. 500, having a lower viscosity, produced filling of the appendix in 91 per cent of the cases, and in 66 per cent filling occurred within 7 hours after the ingestion of the contrast meal.

A second group of experiments were carried out on a series of volunteers from the civil defence barracks at Hillerød, totalling 33 young men, whose ages ranged from 18 to 27 years. However, it soon appeared that from an experimental point of view these volunteers were slightly inferior to the series of patients already described. They were, apparently, mostly young men who had previously suffered from abdominal symptoms and may have reported for the investigation in the hope of having thrown new light on their previous disease. A rather summary questioning to which all were subjected revealed that three of them had previously been in hospital for observation for appendicitis, for which reason they were, obviously, excluded.

Cellugel Super 15,000 was administered as previously described.

Among the subjects studied, filling was observed in 26 instances, or 78.8 %.

For practical reasons, fluoroscopic examinations could be carried out only at 7 and 24 hours after the ingestion of the contrast meal, but according to the experience gained in the first experimental series this should have been sufficient. At the 7-hour examination, filling was observed in 15, *i. e.*, 57.7 %, of a total number of 26 with filling.

By mistake, two subjects were examined twice at a fortnightly interval; exactly the same result was obtained on both occasions: one showed filling at 7 hours and the other at 24 hours.

Repeated examination of the subjects in whom the appendix failed to fill could not be accomplished. In the 26 subjects with positive findings, the appendix filled to the tip in 21 instances (+++); in 4 instances the appendix showed spotted, segmented filling without a visible apical portion (++), and in 1 instance revealed filling only at the base (+). In one case, the appendix pointed laterally and was markedly fixed; the position of the appendix which had shown filling only at the base could not be determined; the remaining cases showed a medial position.

The third group was the smallest; it consisted of 12 women who shortly afterwards underwent operation for some well-defined gynecologic disease. Cellugel Super 15,000 was given in the usual way 24 hours before the operation.

At operation the position and appearance of the appendix were described and the appendix removed en passant. After removal, it was roentgenographed with and without contrast medium, cut open, and subjected to histologic examination.

Of the 12 patients, seven were operated on for ovarian cyst, two for fibroma of the uterus, and three underwent sterilization. In eight of these

patients, roentgen examination had revealed filling of a normal appendix, and in all these cases operation and histologic examination confirmed that the appendix was normal.

The findings in the remaining four cases are briefly reported below.

Report of Cases

Case 1. 1893/52, aged 52, operated on for left-sided ovarian cyst.

Roentgen examination: The appendix lay along the medial wall of the cecum; filling of the proximal half observed.

Histologic examination: Proximally, the appendiceal wall was of normal appearance, apart from marked atrophy of the lymphoid tissue and a few mucosal scars. Distally, the mucosa had been replaced by a narrow cicatricial zone of connective tissue, which continued down into the submucosa. *Diagnosis:* Sequelae of appendicitis with almost complete obliteration of the lumen.

Case 2. 3/46, aged 39, had previously undergone operation for right-sided ovarian cyst and was now subjected to sterilization.

Roentgen examination: The appendix arose from the fundus of the cecum, was directed downwards, and seemed to be completely fixed; filling of the proximal 3—4 cm observed.

Operative finding: The entire cecum and its surroundings were embedded in net-like adhesions; appendectomy not performed.

In both these cases, definite pathologic changes could explain the partial filling of the appendix, and the roentgen and operative findings showed good agreement.

Case 3. 676/52, aged 25, operated on for right-sided ovarian cyst and left-sided ovarian abscess.

Roentgen examination: The appendix failed to fill; examination not repeated.

Histologic examination: The appendix was of medium thickness, with a slightly dilated lumen, and contained some grayish, slightly blood-tinged matter. Marked accumulation of leukocytes in the lumen (slight empyema-like changes). On the serosa there were grayish-red, ragged, adhesion-like areas, but no definite coating. *Diagnosis:* Sequelae of appendicitis and peri-appendicitis.

Case 4. 1694/52, aged 20, operated on for right-sided ovarian cyst.

Roentgen examination: The appendix failed to fill; examination not repeated.

Operative finding: The appendix was found lateral to the cecum with the basal half completely embedded in adhesions.

Histologic examination: The appendix was 8 cm long, with fibrous obliteration of the apical portion. In sections from this portion, the lumen was filled with fibrillated connective tissue. Sections from the remaining part of the appendix showed that the lumen was of medium size. Signs of acute inflammatory changes were not observed. *Diagnosis:* Sequelae of appendicitis and peri-appendicitis with partial fibrous obliteration of the lumen.

It is noteworthy that even though the appendiceal changes observed in Case 3 and, particularly, in Case 4 were not so conspicuous that it

Fig. 1. Complete filling (+++).

Fig. 2. Well-filled, thread-like appendix (+++).

Fig. 3. Same case as in fig. 2, showing change in the position of the appendix.

Fig. 4. Small, thread-like appendix (+++).

might be expected that they would prevent influx of contrast medium into the lumen, they provided, nevertheless, definite evidence of a past history of acute appendicitis.

Fig. 5. Large appendix with segmented filling (++).

Fig. 6. Lateral, proximal position of the appendix (++).

Fig. 7. The fundus of the cecum filled with contrast medium; appendix not visible.

Fig. 8. Same case, 5 minutes later under compression.

To recapitulate, it may be said that the examinations of the 12 patients showed good agreement between the roentgen and operative findings,

since filling was observed in all the normal appendices, whereas either partial or complete failure to fill was seen in the four cases with definite fibrous changes of the appendix.

SUMMARY

Studies on contrast filling of the normal appendix employing special media are reported.

One series of forty-two normal subjects showed filling of the appendix in 97.6 % of the cases, while filling was obtained in 91 % of another series consisting of twenty-two normal subjects.

A series of thirty-three young men called up for military service were also examined; filling of the appendix was observed in 78.8 %.

The appendix failed to fill in four out of twelve women who were subjected to gynecologic operations shortly afterwards. The operative and histologic findings in these four cases are discussed.

ZUSAMMENFASSUNG

Studien über Kontrastfüllung des normalen Appendix unter Benutzung spezieller Kontrastmittel werden berichtet.

In einer Serie von 42 normalen Individen zeigten 97.6 % Kontrastfüllung des Appendix, während dies in einer anderen Serie von 22 normalen Personen in 91 % der Fall war. Eine Serie von 33 zum Militärdienst einberufenen jungen Männern wurde ebenfalls untersucht; Füllung des Appendix wurde in 78.8 % beobachtet.

Der Appendix füllte sich bei 4 von 12 Frauen, die kurz nachher einer gynäkologischen Operation unterworfen wurden, nicht. Die operativen und histologischen Befunde in diesen 4 Fällen werden diskutiert.

RÉSUMÉ

L'auteur rend compte de travaux sur le remplissage de l'appendice normal grâce à des produits de contraste spéciaux.

Sur une série de quarante-deux sujets normaux, l'appendice s'est rempli dans 97.6 % des cas, alors qu'il se remplissait dans 91 % des cas d'une autre série de vingt-deux sujets normaux.

Trente-trois jeunes gens appelés au service militaire ont aussi été examinés; l'appendice s'est rempli dans 78.8 % des cas.

Sur douze femmes qui ont subi des opérations gynécologiques peu après, l'appendice ne s'est pas rempli dans quatre cas. Les constatations opératoires et histologiques faites dans ces quatre cas sont étudiées.

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FROM THE CHITTARANJAN CANCER HOSPITAL, CALCUTTA, INDIA

CHANGES IN THE CELLULAR ELEMENTS OF BLOOD FOLLOWING ADMINISTRATION OF P^{32}

by

Santosh Mitra, K. L. Bhattacharya, A. Bose and
K. P. Chakraborty

The influence of quantity and quality of radiation on the cellular elements of the blood has been the subject of extensive studies (TUTTLE et al., 1939 and ABELS et al., 1941). The effect of protraction of radiation over different periods has also been investigated. It has been found that the degree and the type of the damage is greatly influenced not only by the total dose but also by the size of the individual dose and the interval between them (GLASSER et al., 1945). Most of this work has been carried out with the radiation from radium, with a view to find out the best combination of fractionation and protraction of dosage for the production of the desired clinical response.

Radioactive isotopes such as P^{32}, Na^{24} etc., are now used extensively in therapy and tracer work. When these radioisotopes are used internally there is continuous whole-body irradiation. The effect of such continuous irradiation on the haemopoietic system from radioisotopes deposited internally on various organs is different from that of roentgen rays and the radiation from radium employed externally. In the present paper an account is given of an investigation on the effects of whole-body irradiation with P^{32} on the cellular elements of blood when P^{32} was applied in different doses.

Materials and Methods

Adult white albino rats were used throughout this series of experiments. Thirty rats were divided into five groups of six each. They were given single intraperitoneal doses of Na_2HPO_4 containing P^{32}; the doses were 0.3 μc/gm, 0.5 μc/gm, 1.0 μc/gm, 2 μc/gm, and 4.5 μc/gm of body weight respectively.

Submitted for publication, March 2, 1953.

P^{32} used in these experiments was obtained from the Atomic Energy Research Establishment, Harwell in the form of carrier-free soluble Na_2HPO_4. The strengths of the samples were specified by the Atomic Energy Research Establishment, but in order to avoid any accidental error, the strengths of the solutions just before injection were rechecked against a simulated P^{32} reference source containing Ur^{238} in secular equilibrium with Thorium^{234} and Protoactinium^{234}. This combination having almost infinite half-life and the same spectral distribution of beta-rays as P^{32}, and previously calibrated against a U. S. Bureau of Standards P^{32} solution, served as the simulated standard. End-window type of Geiger Müller counters and scaling circuits made by Tracerlab Inc., Boston, were used in this work. The strengths of the samples as given by Harwell specifications and those derived from our measurements with the help of a Bureau of Standard Reference source, always agreed within 1 per cent.

The experimental animals were first kept under observation under standard diet and laboratory conditions for a few days prior to the administration of P^{32}. The pre-radiation blood count was carried out regularly in this period. After the injection of P^{32}, peripheral blood was drawn from the tails of the animals and both total and differential counts done every fourth day. Great care was taken in order to maintain the same conditions through the experiment as regards food etc. Blood changes of few normal rats without any radioactive phosphorus, were also followed during this period and served as control. In cases of doubt about the blood counts being affected by any extraneous factor such as infection etc., the counts were rejected and the whole series repeated from the beginning.

Observations

A. Variation of Blood Counts with days: The initial pre-radiation counts of the individual rats varied a great deal. The following table gives the average values for the thirty rats involved in the present series of experiments.

Table 1

Average Counts of the Cellular Elements with Standard Deviations

R. B. C.	6.3 ($\pm$ .99)	Million per cu. mm.
W. B. C.	8.4 ($\pm$ 2.12)	Thousand per cu. mm.
Lymphocytes	60.8 ($\pm$ 11.9)	per cent.
Polymorphs	36.0 ($\pm$ 11.8)	per cent.
Monocytes and Eosinophils	3.2	per cent.

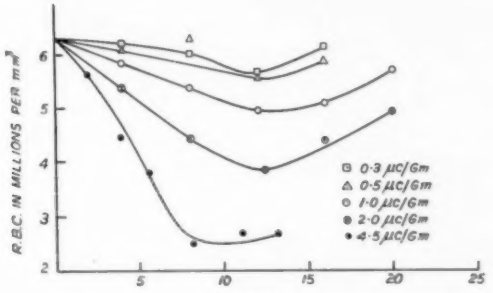

DIAGRAM 1

Diagram 1.

Variation in R. B. C. counts with days following administration of P^{32}.

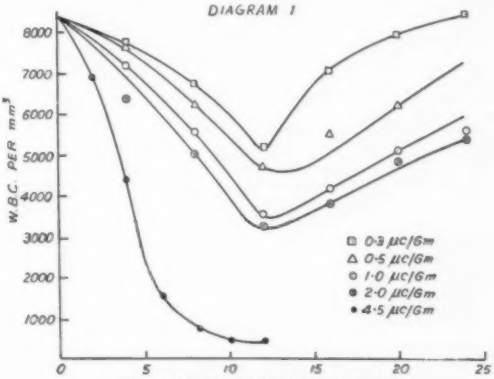

DIAGRAM 2

Diagram 2.

Variation of W. B. C. counts with days following administration of P^{32}.

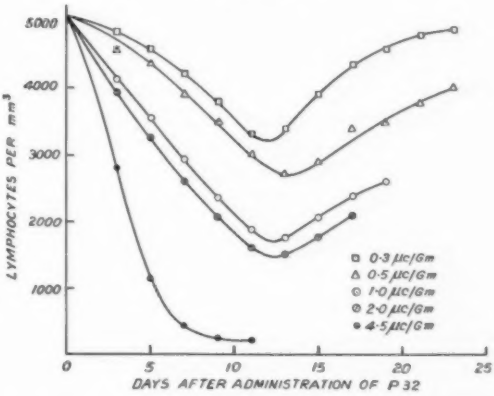

Diagram 3.

Variation in total lymphocyte counts plotted with days following administration of P^{32}.

The progressive decline in the RBC, WBC, and lymphocytes with days after injection of different doses of radio-phosphorus, is shown in diagrams 1, 2 and 3. In representing the results, the mean variation in each

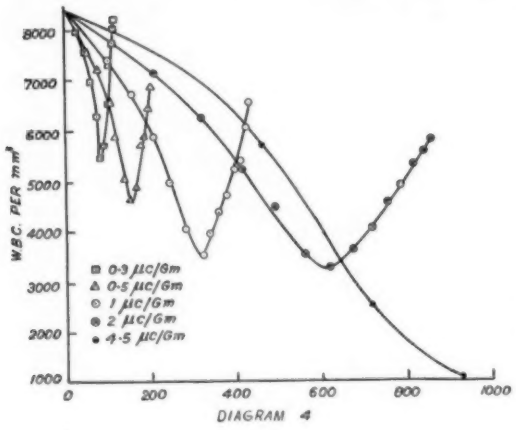

Diagram 4.

Variation in total W. B. C. counts as a function of the accumulated β-dose from P^{32}.

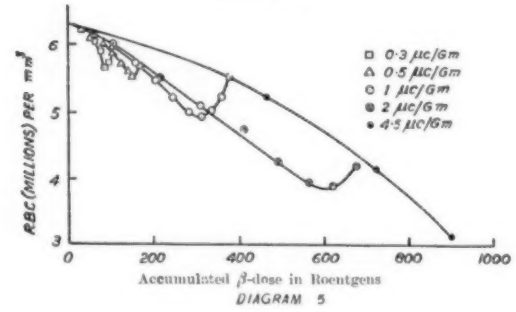

Diagram 5.

Variation in R. B. C. counts as a function of the accumulated β-dose from P^{32}.

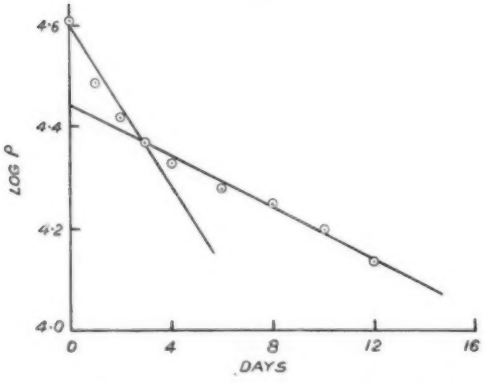

Diagram 6.

Logarithm of percentage activity in the system plotted as a function of days following intraperitoneal injection of P^{32}.

group of rats was first determined. These mean group-variations have been shown in the above figures, with reference to the average initial pre-radiation count given in table 1.

These results revealed that both the WBC and RBC were affected to different extents by the injected radio-isotope. The maximum drop in the counts occurred between the 12th and the 14th day after the administration, after which there was progressive recovery excepting in the case of rats receiving 4.5 μc per gram of body weight. All rats receiving 4.5 μc/gm died within 12 days following the administration of radio-phosphorus.

B. Variation of the Blood Count as a Function of the Accumulated Beta dose:

An attempt was next made to correlate the observed blood changes with the accumulated dose of radiation received by each group of animals due to the absorption of beta rays emitted from the P^{32} injected. In estimating the rate of accumulation of the beta dose an account was taken of the excretion and the rate of uptake by the tissue. All rats in one group had the same concentration of radioactive phosphorus per gram of tissue and hence the same rate of accumulation of the beta dose. Diagrams 4 and 5 show the decrease in the WBC and RBC as a function of the accumulated beta dose, for the five groups of rats receiving 0.3, 0.5, 1.0, 2.0, and 4.5 μc per gram of tissue. The details of the calculation of the accumulated beta dose are given in appendix.

An inspection of the curves of diagrams 4 and 5 shows that the same total dosage of beta-radiation does not always give rise to the same lowering in blood counts. The rate of decrease in blood count per roentgen was maximum in the case of rats injected with 0.3 μc/gm of P^{32}, while it was minimum for rats injected with 4.5 μc/gm, although the last dose was lethal. Since the rats injected with 0.3 μc/gm accumulated the same total β-dose at a much slower rate than the groups receiving 0.5, 1.0 or 2 μc/gm of body weight, this observation means that radiation is more effective in the lowering of blood counts when applied continuously at a slower rate. The same effect is also observed in another form when the total beta dose at which the minimum blood count occurred is considered. It is seen that the minimum count occurred at the higher total beta dosage when the concentration of radioactive material was greater. The detailed significance of these observations is discussed later.

Discussion

The vulnerability of the haemopoietic system to ionizing radiations has long been established by animal experiments and by the damage which has been manifested in those occupied in handling radioactive material. With sufficient doses of radiation either administered internally or applied externally all the cellular elements of the blood are affected.

The general nature of the curves of diagrams 1, 2, and 3 is similar to those obtained by EVANS and QUIMBY (1946) after whole body irradiation of mice with roentgen rays and injection of Na^{24}: there is an initial lowering of the counts and then a slow and steady recovery. All blood cells are found to be affected although to different degrees.

The relative sensitivities of the various cellular elements of the blood, may be inferred from the following table which gives the minimum counts reached with different doses of P^{32}.

Table 2

Minimum Count Reached as Percentage of the Pre-radiation Value

	Minimum count as per cent of the pre-radiation value.			
Dose of P^{32}	RBC	WBC	Lymph	Poly
0.3 μc/gm	89	64	62	62
0.5 μc/gm	88	54	53	52
1.0 μc/gm	78	41	31	48
2.0 μc/gm	61	38	29	49

Thus the lymphocytes seem to be most sensitive to radiation and R.B.C the least. The daily dose received by the animals is proportional to the amounts injected, but this dose varies as the amount in the system decreases. With the help of equation (8) (Appendix) the accumulated dose over the first twenty days was calculated. This dose divided by the number of days indicated the average daily dose at which the animals were irradiated. This average daily dose for the four curves of figures 4 and 5 were approximately as follows:

Table 3

Variation of Average Daily Dose with Concentration

Concentration	Daily dose (Average)
0.3 μc/gm	6.0 rep
0.5 μc/gm	9.5 rep
1.0 μc/gm	19.0 rep
2.0 μc/gm	38.0 rep
4.5 μc/gm	85.0 rep

The diagrams 4 and 5, therefore, represent the changes in the cellular population of blood with the same total β-dose, when the radiation is delivered continuously at different dosage rates. From the nature of the curves, it is evident that the dosage rate plays an important part in the lowering of the blood counts. For example for a total of 100 rep, the number of leukocytes present was 92, 88 and 79 % of the pre-radiation value when radiation was delivered at the rate of 40, 19 and 8.5 rep per day, respectively. Although the counts were lowered in every case with the

increasing cumulative dose, the amount of lowering from the pre-radiation value was dependent on the rate at which the dose was applied. For a continuous application of radiation, the same dose was more effective in the lowering of blood counts when it was distributed over a longer duration of time.

This may be explained by the fact that of the cellular population at any time only a fraction is sensitive to radiation. The effect of ionizing radiation is exerted more upon the dividing cells than upon those that have completed division. Blood cells are not damaged or destroyed as they circulate; actually, in circulation they appear to be remarkably radioresistant (WHITBY 1950). What is observed in peripheral blood is mainly cells which have escaped damage and others which, being badly damaged have been unable to mature at all. Hence if the same dose of radiation is distributed over a greater length of time, it can influence a greater number of dividing cells than when the same dose is applied over a shorter period. This damaging effect of ionizing radiation on cell maturation also explains the fact that the radiosensitivity of cells is directly proportional to their life cycle. The lymphocyte, for example, has been found to be most radiosensitive and its life in circulation is only a few hours while that of the erythrocyte is many days. (VAN DYKE et al. 1951.)

A family of curves of the same nature as those of the W.B.C (diagram 4) may be drawn for lymphocytes. Apart from the fact that they are more sensitive to radiation and the drop in counts is greater than in the total W.B.C, there are no other striking features. The changes in the R.B.C with cumulative dose is shown in diagram 5. The variation in count with accumulated dosage is much less drastic here than in the previous case.

KOLETSKY and CHRISTIE (1951) and HENSHAW (1943), reported early leukocytosis following radiation. This was not confirmed in our case. This might be due to the fact that no count was made earlier than the third day after the administration of P^{32} and the early leukocytosis, if there was any, within the first 3 days, was missed. This idea was contradicted by JACOBSON et al. (1949).

Appendix

Calculation of the Intergal beta-ray Dose due to different Amounts of Injected Radiophosphorus

We assume that 1 roentgen, corresponding to the release of 1 E. S. U. charge per c.c. of air at 0° c and 760 mm pressure, is equivalent to the release of an energy of 5.2×10^{13} electron volts per gram of air.

Radioactive phosphorus P^{32} has a physical half-life of 14.3 days corresponding to a disintegration constant of $\lambda = .0485$ days^{-1}. When the radio-isotope is injected into a rat the radioactive atoms are distributed throughout the system, producing an initial uniform concentration. As the time interval during which this initial equilibrium is

reached is negligible, the rate of accumulation of the beta dose will be calculated for an initial concentration of 1 microcurie per gm of tissue.

The radioactive atoms are lost from the system due to two competitive processes: physical decay and the biologic excretion. Let the probability of loss per day by the second process be denoted by λ_β. Then if No be the number of atoms corresponding to an activity of 1 μc of P^{32}, the number N(t) left after a time t is given by

$$N(t) = No\, e^{-(\lambda + \lambda_\beta)t} \quad \ldots\ldots \quad (1)$$

Out of these, the number of atoms disintegrating within a time interval t and $t + dt$ is

$$\lambda N(t)\, dt = \lambda No\, e^{-(\lambda + \lambda_\beta)t}\, dt \quad \ldots\ldots \quad (2)$$

Total number of beta rays emitted during the interval o—t is given by

$$\int_0^t \lambda N(t)\, dt = \frac{No\,\lambda}{\lambda + \lambda_\beta}\left[1 - e^{-(\lambda + \lambda_\beta)t}\right] \quad \ldots\ldots \quad (3)$$

If the average beta particle energy is $\bar{E}_\beta$ in electron volts, then the cumulative beta dose at a time t, corresponding to an initial uniform concentration of 1 μc of P^{32} per gm of tissue, is

$$D_\beta = \frac{No\,\lambda}{\lambda + \lambda_\beta}\left[1 - e^{-(\lambda + \lambda_\beta)t}\right]\frac{\bar{E}_\beta}{5.2 \times 10^{13}}\ \text{rep} \quad \ldots\ldots \quad (4)$$

Introducing the effective half-life

$$T_E = \frac{.693}{\lambda + \lambda_\beta} \quad \ldots\ldots \quad (5)$$

$$D_\beta = \frac{No\,\lambda\, T_E}{.693}\left[1 - e^{-(\lambda + \lambda_\beta)t}\right]\frac{\bar{E}_\beta}{5.2 \times 10^{13}} \quad \ldots\ldots \quad (6)$$

for 1 μc, $No\lambda = 3.7 \times 10^4$ and $\bar{E}_\beta = .7 \times 10^6$ e. v. for P^{32}, and if T_E is expressed in days, we have

$$D_\beta = 61.6\, T_E\left[1 - e^{-.693\frac{t}{T_E}}\right] \quad \ldots\ldots \quad (7)$$

The rate of accumulation of beta dose for an initial concentration of Co μc/gm is given by

$$D_\beta = 61.6\, T_E\left[1 - e^{-.693\frac{t}{T_E}}\right] Co \quad \ldots\ldots \quad (8)$$

With the help of equation (8) the cumulative beta dose at any time t after the injection of radio-phosphorus may be estimated provided the effective half-life T_E is determined experimentally.

In a separate experiment, the same doses of radioactive material as used in the present experiment, were injected into another set of rats. The total radioactivity in the excretions was measured at regular intervals. The results of this series of experiments showed that the excretion was very rapid during the first three days following the injection, after which it slowed down. The microcuries excreted were converted into a percentage of the administered dose; from this the percentage of the dose administered remaining in the system (P) was calculated, the biologic loss only being taken into consideration. The logarithm of the activity remaining in the system (Log. P) when plotted against days,

fell on two straight lines with different slopes (diagram 6). From the slopes of these lines and taking the physical half-life of P^{32} (14.3 days) into consideration, the effective half-life (T_E) for the first three days was found to be 5.4 days and for the remainder of the period 9.4 days. LOWBEER et al. (1952) found values of 8 and 11 days respectively for these H. L. D. following the intravenous injection of P^{32} in human subjects.

Acknowledgements

This work was made possible by grants from the Atomic Energy Commission, Government of India. The authors are greatly indebted to Dr. N. N. DAS-GUPTA for directing the investigations and to Dr. S. P. RAY-CHAUDHURI and Dr. R. DATTA-CHAUDHURY for helpful criticisms. They also records their thanks to Dr. SUBODH MITRA, Director Chittaranjan Cancer Hospital, for his interest in this study.

SUMMARY

Changes in the cellular elements of the blood of white albino rats following the administration of doses of P^{32}, varying from 0.3 μc/gm to 4.5 μc/gm, were studied. Doses up to 2 μc/gm were found to be sublethal: all rats receiving 4.5 μc/gm died within 12 days.

The radiosensitivity of the blood cells was directly proportional to their life cycle. The amount of lowering of the count of different cellular elements was influenced appreciably by the rate at which the beta dosage was applied.

ZUSAMMENFASSUNG

Veränderungen der Zellelemente des Blutes bei weissen Albinoratten nach Administrierung von zwischen 0.3 μc/gm bis 4.5 μc/gm schwankenden Dosen P^{32} werden studiert.

Dosen bis zu 2 μc/gm wurden als sublethal befunden; alle Ratten, die 4.5 μc/gm erhielten, starben innerhalb von 12 Tagen.

Die Strahlenempfindlichkeit des Blutes war dem Lebencyklus der Ratten direkt proportional.

Die Grössenordnung der Verminderung der Anzahl der verschiedenen Zellelemente wurde wesentlich von den Ratten bestimmt, bei denen die Betadosis angewendet wurde.

RÉSUMÉ

Les auteurs ont étudié les modifications des éléments cellulaires du sang, chez des rats albinos blancs, après administration de doses de P^{32} allant de 0.3 μc/g à 4.5 μc/g.

Jusqu'à 2 μc/g, les doses se sont montrées subléthales; tous les rats qui avaient reçu 4.5 μc/g moururent dans les 12 jours.

La radiosensibilité des cellules sanguines s'est révélée directement proportionnelle à leur cycle de vie.

L'importance de la diminution du nombre des différents éléments cellulaires est sensiblement influencée par les rats qui ont reçu la dose bêta.

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FROM THE DEPARTMENT OF RADIOTHERAPEUTICS (DIRECTOR: PROFESSOR J. S. MITCHELL)
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EXPERIENCE WITH THE 30 MeV SYNCHROTRON AS A RADIOTHERAPEUTIC INSTRUMENT

III. Approach to clinical use

by

J. S. Mitchell, C. L. Smith, D. J. Allen-Williams and *R. Braams*

The only satisfactory test of a new type of medical treatment is the practical one of using it. A final assessment of the value of 30 MeV_p roentgen radiation, or of any promising new method in radiotherapy requires the treatment of large numbers of patients suffering from each selected site and type of cancer with follow-up for at least five years, and preferably longer. However, it is essential to estimate the value of the new method of treatment as economically as possible before advising its use on a large scale. This involves a statistically planned comparison of the results of treatment of patients during the same period with 30 MeV_p roentgen rays and with some well understood standard form of treatment such as filtered 220 kV_p roentgen radiation.

An investigation of this type is envisaged, but at present we are at the stage of preliminary exploration. On account of the technical difficulties with our synchrotron, it was evident that facilities for clinical trials of its use were likely to be limited, at least temporarily. Accordingly we have concentrated on the radical treatment of a few patients with histologically verified malignant tumours occurring at sites for which radiotherapy by the usually available methods is unsatisfactory. It seemed reasonable to select patients with lesions in which the probability of permanent cure is low and difficulty of accessibility appears to be an important factor limiting radiocurability.

There is some published information about the therapeutic use of roentgen rays of energy in the region of 20—30 MeV. There is no reason

Submitted for publication, February 7, 1953.

to anticipate any differences between the effects of the roentgen rays of the same energy produced by the betatron and by the synchrotron. The first clinical application of the betatron was on 30th April, 1948, at Urbana, Illinois, when 22 MeV roentgen radiation was used to try to help a patient with an inoperable cerebral tumour which had not improved after 800 kV roentgen therapy. The patient died but the account of the techniques developed (QUASTLER et al. 1949) is an important contribution which has greatly influenced subsequent workers in this field. An account of preliminary clinical experience in the treatment of 17 patients with 23 MeV roentgen rays from a betatron at Chicago was given by HARVEY, HAAS and LAUGHLIN (1951). WATSON and BURKELL (1951) have reported on the treatment of 75 patients with 22 MeV roentgen rays produced by the betatron at the University of Saskatchewan. SCHINZ and WIDERÖE (1952) have described the 31 MeV betatron installed for radiotherapy at the Zurich Cantonal Hospital and have reported on the treatment of 44 patients.

Short reports on the clinical use of the 30 MeV synchrotrons at the Royal Cancer Hospital, London and at Cambridge were included in the Annual Report of the British Empire Cancer Campaign for 1951 (p. 39, 49, 289).

Problem of Relative Biological Efficiency

For practical radiotherapy, it is essential to determine the value within $\pm$ 10 % of the ratio of the doses of filtered 200—250 kV roentgen rays and of filtered 30 MeV_p roentgen rays which produce equal biological effects on normal tissues and malignant tumours, when used with similar time and intensity factors. In comparing these radiations, from the biophysical point of view the most important factor is probably the specific ionisation of the secondaries (Cf. GRAY 1946, 1947). The question must be raised of the possible influence on the biological actions of the ultrafractionation of the 30 MeV_p roentgen rays; however, it appears unlikely that this factor introduces any large effects.

Calculated values of the approximate mean specific ionisation of the secondaries in water are given in Table I for a number of qualities of radiation used in radiotherapy; the most significant values are probably those of CORMACK and JOHNS (1952). However, without attaching great importance to the actual numerical values, it is evident that there is little difference to be expected between the specific ionisation of the secondaries produced by 20—30 MeV roentgen rays and by the γ-rays of radium and radio-cobalt. Filtered 220 kV_p roentgen rays show substantially higher values. For 800—1,000 kV roentgen rays and radio-iridium γ-rays, the specific ionisation of the secondaries has values which

are intermediate but lie much closer to those of the high energy than of the low energy radiations.

Accordingly, *a priori* evidence suggests that in radiotherapy the biological effects per unit dose are likely to be substantially the same for 30 MeV_p roentgen rays and radium γ-rays.

It seems reasonable to expect that for the production of equal effects on deep tissues, the dose of 30 MeV_p roentgen rays required will be approximately 1.4 ± 0.1 times that of the usual filtered 200—250 kV roentgen rays when used with comparable overall time, fractionation and exposure times. Moreover, with 30 MeV_p roentgen rays in comparison with radium γ-rays there is no reason to anticipate either any loss of differential selective action between normal and malignant cells, or unusually severe late reactions of the type observed by STONE (1948) after fast neutron therapy.

The preliminary reports of the clinical trials by HARVEY, HAAS and LAUGHLIN (1951), WATSON and BURKELL (1951) and SCHINZ and WIDERÖE (1952) show that substantially higher tumour doses are required with 25—31 MeV_p roentgen rays than with 200—250 kV roentgen rays. As yet there appears to be insufficient clinical evidence to determine the ratio with confidence.

To obtain further information about this problem a number of animal experiments using 20—31 MeV_p roentgen rays have been carried out. These include studies of acute lethal effects in mice (QUASTLER and CLARK 1945), decoloration of hair in mice (CHASE, QUASTLER and SKAGGS 1947), induction of sex-linked recessive lethal mutations in Drosophila (LUCE, QUASTLER and SKAGGS 1949), lethal effects on Drosophila eggs (FREY 1952), and the production of leukopenia in mice (TING, JOHNS and JAQUES, 1952). It is of interest that the last mentioned authors found that the ratio of effectiveness in producing 70 percent leukocyte reducrion for filtered 23.5 MeV roentgen-rays to 200 kV roentgen radiation of H. V. L. 1.4 mm Cu for three strains of mice was 0.65, corresponding to a value of 1.54 for the reciprocal ratio.

The intensity of the roentgen ray beam from the Cambridge synchrotron has been too low for experiments on animal tumours. Meanwhile, cytological experiments have been made with *Tradescantia bracteata* microspores by Mr. K. C. BORA. Details will be published elsewhere, but the following example of information obtained is of interest. The cytological effects of doses of 300 r delivered at the rate of 3.3 r per minute were compared for three radiations: (A) 220 kV_p roentgen rays, H. V. L. 2.5 mm Cu, (B) Ir^{192} γ-rays, and (C) filtered 30 MeV roentgen rays. (See Table I.) The percentage of damaged cells observed was respectively 50.4 ± 3.3, 33.1 ± 2.3 and 31.0 ± 2.3. It is relevant to note that in

these experiments there was no significant difference between the effects of the Ir^{192} γ-rays and of the 30 MeV roentgen rays.

Table I

Radiation	Effective mean energy MeV	Calculated values of approximate mean specific ionisation of secondary electrons; ion pairs per micron of track in water		
		(1)	(2)	(3)
220 kV_p roentgen rays. H. V. L. 1.5 mm Cu...	0.100		66	
220 kV_p roentgen rays. H. V. L. 2.25 mm Cu .	0.120		60	
220 kV_p roentgen rays. H. V. L. 2.5 mm Cu...		80		46
Radio-iridium, Ir^{192}, γ-rays & 800 kV roentgen rays. H. V. L. 8.5 mm Cu	0.40		14	
1,000 kV roentgen rays. H. V. L. 9.5 mm Cu..	0.52	15	10	
Radium γ-rays, filtered by $^1/_2$ mm Pt	0.8	11	7.5	7.4
Radio-cobalt γ-rays.....	1.25	11		7.8
25 MeV roentgen rays, filtered		8.5		6.2
30 MeV roentgen rays, filtered	7.6 [1]		6.5	

(1) See GRAY (1947).
(2) See MITCHELL (1945).
(3) CORMACK and JOHNS (1952).

Treatment of Patients

We have only been able to treat 5 patients between May 1951 and March 1952. We have started with cases treatable by a single field technique as the simplest method of utilising the characteristic properties of 30 MeV_p roentgen rays and of assessing the tissue reactions. The fixed roentgen ray beam is inconvenient but ample use has been made of our experience with routine methods for accurately localised small volume irradiation.

At this stage it may be of interest to report in some detail on three illustrative cases, including comparison with conventional radiotherapy (Cases 1, 2, and 3).

Two other patients were treated. One was a professional man of 39 who had an incomplete surgical removal of a chordoma arising in the region of the right side of the body of the sphenoid; he was the first patient to be treated with our synchrotron and his treatment started on 5. 5. 51. The lesion was histologically of low malignancy and appeared to be radiosensitive. The patient returned to full work after about 4 months

[1] Energy of monochromatic radiation corresponding to the value of 0.0248 cm^2/g for the mass absorption coefficient of water.

and since then has lived an exceedingly busy and active professional life. The other patient was a housewife of 31 who had a partial removal of a glomus jugularis tumour of the right middle ear, for which she received radical post-operative 30 MeV_p roentgen therapy, with a good immediate result.

Case 1. A. H. 51327. Male. Age 45 years. Storekeeper. Inoperable cerebral tumour — right temporo-frontal region.

History: First symptom: drowsiness in June 1951. In August 1951, he had four major epileptic attacks with intermittent dizziness and paraesthesiae of the left arm and leg. *Relevant previous history:* Discharge from the left ear since the age of 9. Operation left mastoid in 1942; since then he has still had continual otorrhea with granulations in the left external auditory meatus. *Special Investigations:* Neurological examination showed only a very mild left lower motor neurone type of facial paresis. No papilloedema.

Films of the skull showed a small area of eroded bone just above the right pterion exactly over the site of the tumour. The right internal carotid arteriogram showed displacement upwards of the middle cerebral artery, suggesting a right temporal tumour. Ventriculography confirmed a right temporal lesion.

Operation: 22. 11. 51. (Mr. V. Logue): glioma felt in right tempor-frontal region. Because the tumour extended into the frontal lobe it was not suitable for temporal lobectomy. The only surgery was a biopsy. *Histology:* Glioblastoma multiforme (Dr. J. H. Dean). *Examination:* 30. 11. 51. General condition surprisingly good. Mentally alert. Skull extraordinarily asymmetrical. Moderate left facial paresis. Slight left papilloedema. *Action:* In view of the poor prognosis associated with the histology and the good general condition of the patient, it was considered justifiable to attempt radical treatment with the synchrotron with conservative dosage.

Radiotherapy: Synchrotron. Radical 30 MeV_p roentgen therapy (incomplete). Single right temporo-frontal field 7.5 cm diameter cut off anteriorly with 2″ lead brick "eye-shield". Beam direction. Field position checked radiographically. The tumour was considered to be of dimensions 6.8 cm laterally by 6.2 cm anteroposteriorly and vertically and lies well within the 90 % isodose surface, taking into account the absorption in the bone. 15 treatments 13. 12. 51—31. 12. 51. At this point the treatment was discontinued because of headache and nausea. Total minimum tumour dose 90 % = 3,220 "r" in overall time 18 days. *Reaction:* 1. 1. 52. Right side, only the faintest erythema but epilation over a circular area 8.0 cm diameter. Left side — epilation over an area about 8.5 cm diameter, but erythema more extensive over a circular area 10.0 cm diameter, and slight dry desquamation. No blood count changes at any stage. *Progress:* Great improvement. Rapid disappearance of left papilloedema. Occasional epileptiform seizures decreasing in frequency, the last attack being during the night of 23rd April, 1952. He returned to work full time as storekeeper, taking phenobarbitone g 1 each night, and when seen on 13. 8. 53 was very well.

Comparison with conventional radiotherapy.

At 30 MeV_p and F. S. D. 100 cm for a single lateral field 7.5 cm diameter, with the 5 cm thick lead "eyeshield" anteriorly, the tumour dose lay between 90 and 100 %, while the skin dose was about 20 % at entry and about 70 % at exit. The dose at the adjacent cerebral cortex did not exceed 80 % and there was a rapidly falling dose outside the geometrical beam. The integral dose was approximately 970 g "r" per minimum tumour "r" taken as 90 %.

At 220 kV_p, H. V. L. 1.5 mm copper and F. S. D. 50 cm a reasonable field arrangement would have been a 3-field one with two opposing lateral fields 10 × 10 cm^2 at 14 cm

apart together with an anterior field 7 cm wide by 10 cm vertically. All fields receive 100 % of the applied dose. Then the tumour lies between 120 and 140 % while the skin dose is about 130 % on the side of the tumour, just reaches 120 % on the opposite side and is about 100 % anteriorly. Most of the cerebral hemispheres except the occipital lobes would be irradiated above the 90 % level. The integral dose would be approximately 2,720 g r per minimum tumour r at 120 %.

Case 2. A. H. 5503/47. Male. Age 63 years. Night Watchman.

(1) Carcinoma of soft palate with extension to left lateral pharyngeal wall. No glands.

(2) Pernicious anaemia, treated with liver and iron, and recently with Vitamin B 12.

History: First symptom: sore throat in April 1951. Ulcer on soft palate noticed by physician treating pernicious anaemia. *Relevant previous history:* Pernicious anaemia diagnosed in 1947, responded well to liver and iron therapy and recently controlled apparently completely by Vitamin B 12, 50 micrograms every 3 weeks. *Examination:* 31. 10. 51. General condition not very good. Rather thin and wizened, looking much older than his age. No anaemia. Gross ulceration and destruction of soft palate starting near the midline and extending on both sides but especially on the left side where the ulceration has spread on to left lateral pharyngeal wall. The lesion is about 5 cm in diameter including the whole of the extension on the left side. No glands palpable. W. R. negative. The lesion extends from depth 3—8 cm below the skin on the left side. *Histology:* Moderately well-differentiated squamous carcinoma with fairly numerous mitoses. *Action:* There was no possibility of treatment by radical surgery or a radium implant. Beam therapy — in our case with the radio-iridium teletherapy unit — and therapy with heavily filtered 220 kV_p roentgen rays were possible but experience of these forms of treatment in similar advanced cases, despite the absence of secondary nodes, has been very unsatisfactory. Accordingly it was considered justifiable to attempt radical treatment with the synchrotron.

Radiotherapy: Synchrotron. Radical 30 MeV_p roentgen therapy. Single left lateral oropharyngeal field 7.5 cm diameter. Centre points for beam direction 2.0 cm above point of mandible on bony posterior margin of mandible. D (RL) = 11 cm. The tumour lies within the 95 % isodose surface. First course of treatment: 26. 11. 51—7. 12. 51. 9 treatments in 11 days. Total minimum tumour dose 95 % = 3,672 "r". Treatment was stopped because of astonishingly early mucosal reaction. He rapidly became ill and dehydrated, and was admitted as an emergency on 10. 12. 51. There was a slight pink erythema over a circular area 7 cm diameter on the left (entry) side, with a dusky erythema over an area 10 cm diameter on the right (exit) side. Lymphocytopenia reaching 210 per mm^3 on 17. 12. 51. After intravenous glucose saline, he improved rapidly. The growth shrank but there was a very obvious residue. A further course of treatment was started 31. 1. 52. 14 treatments were given in this course, the last on 16. 2. 52. Additional total minimum tumour dose, 95 % = 2,736 "r" in 16 days. Despite all this treatment and the gross local infection for which he was given intensive penicillin treatment, the lesion continued to grow and appeared to extend. 6. 3. 52. Local lesion obviously still widely active. No glands.

The lesion never healed. The tumour response was unsatisfactory despite the very severe reaction of the normal tissues. The question is raised as to whether the tumour response was reduced by the Vitamin B 12. After a few weeks apparently the tumour started to grow again.

Died 15. 4. 52. No autopsy. Certified cause of death — Carcinoma of palate; Pernicious anaemia.

Comparison with conventional radiotherapy.

At 30 MeV_p and F. S. D. 100 cm, for a single lateral field 7.5 cm diameter, the tumour dose lay between 95 and 100 %, while the skin dose was about 20 % on the entry side and about 85 % at exit. The integral dose was approximately 730 g "r" per minimum tumour "r" taken as 95 %.

At 220 kV_p, H. V. L. 1.5 mm copper, and F. S. D. 50 cm with two opposing fields 7.5 cm diameter at 11 cms apart, the tumour dose lay between 90 and 115 % and the entrance skin dose was 125 %. The integral dose was approximately 950 gm r per minimum tumour r at 90 %.

Case 3. A. H. 5295. Female. Age 66 years. Housewife. Inoperable carcinoma of left parotid gland. Previous unsuccessful 220 kV roentgen therapy (two courses). Intensive palliative 30 MeV_p roentgen therapy. Pulmonary metastases. *Histology:* Anaplastic carcinoma of salivary gland. (Aspiration biopsy.)

History: First symptom: swelling of left side of face in August 1948. Slowly progressive increase in size of swelling of left parotid gland. First referred 28. 3. 49; there was then a left parotid tumour with diffuse bulging of the left side of the soft palate. No glands. Sialogram negative. Roentgen therapy: 220 kV_p H. V. L. 1.5 mm copper. Left parotid field 7.5 cm diameter. Spaced treatment: 1. 11. 49—9. 12. 49. Skin dose 4,500 r, minimum tumour dose at 5 cm, 52.5 % = 2,365 r. There was then considerable reduction in the size of the swelling and improvement but recurrence of growth occurred in the deep part of the tumour in July 1950, as confirmed by examination under anaesthesia.

Further radical roentgen therapy: 220 kVp, H. V. L. 1.5 mm copper. Two opposing facial fields 7.5 cm circles centred 1.0 cm anterior to external auditory meatus. Beam direction. Spaced treatment: skin dose 3,400 r. Central dose 2,700 r. 24. 7. 50 to 11. 8. 50. Supplementary left submaxillary field, 7.5 cm diameter circle. 5 treatments: 28. 8. 50—1. 9. 50 to bring minimum tumour doses up to 3,700 r in this course.

There was temporary improvement, but from about September 1951 she had increasing pain and paraesthesia in the second and third divisions of the left trigeminal with a slowly progressive left facial paralysis of lower motor neurons type.

Examination: 4. 2. 52. General condition rather poor. There was a recurrent mass about 6 cm diameter with extension to the pharynx and protrusion into the external auditory meatus: also a fixed mass 4 cm diameter below and behind the angle of the mandible and involvement of the following cranial nerves V(2), V(3), VII, VIII, X (fixed left vocal cord) and XII. Almost certain involvement of the masseter muscle; the jaws opened 3 cm only. Active growth about 6 cm in diameter confirmed by radiography as a sphere lying between 2 and 8 cm from the surface of the raised mass on the left side. 29. 1. 52. Films of chest showed early pulmonary metastases. *Action:* Despite the early symptomless pulmonary metastases, it was essential to give further palliative radiotherapy to try to relieve her increasing pain and misery. Further 220 kV roentgen therapy was impossible. Accordingly the use of 30 MeV_p roentgen rays was regarded as justifiable.

Radiotherapy: Synchrotron. Intensive palliative 30 MeV_p roentgen therapy. Single 7.5 cm diameter circular field. Entrance point on the left side 3 cm above angle of jaw, exit on the right side 1.5 cm above angle of jaw. Radiographic checking of beam direction. The tumour lies within the 90 % isodose surface. 22 treatments: 31. 1. 51—28. 2. 52. Estimated total minimum tumour dose, 90 % = 3,930 "r" in 28 days. *Reaction:* After 11 treatments she felt sick and giddy and collapsed. It is very doubtful whether this was in any way a radiation reaction. Lymphocytes fell to 400 per mm^3 on 26. 2. 52. There was no skin reaction on the left side. There was dry desquamation with some pigmentation on the opposite side. The tumour mass retrogressed slightly externally, but very

considerably internally. This made her very much more comfortable. *Progress:* 9. 7. 52. Pain in left parotid region, but no chest symptoms. There was a tiny breaking down skin area over the parotid tumour almost certainly due to the large amount of radiation given at various times in this region. Her general condition had slightly deteriorated and she then had paralysis of the left side of the soft palate. Fortunately she had no pulmonary symptoms. 15. 8. 52. Surprising improvement. 29. 10. 52. Improvement maintained with no symptoms.

Comparison with conventional radiotherapy.

At 30 MeV_p and F. S. D. 100 cm, for a single lateral field 7.5 cm diameter, the tumour dose lay between 90 and 100 % while the skin dose was about 20—80 % over the projecting tumour and about 75 % at the exit surface. The integral dose was approximately 970 g "r" per minimum tumour "r".

At 220 kV_p, H. V. L. 1.5 mm copper and F. S. D. 50 cm, the technique used successfully in a very similar case was a convergent 3 field one using a specially made former, with three 7.5 cm diameter circular fields at 50 % to the axis of the tumour and at 120° to each other. The tumour dose lay between 120 and 140 % and the skin dose reached about 130 %. The integral dose was approximately 1,040 g r per minimum tumour r at 120 %.

Discussion

The main advantages of the use of 30 MeV_p roentgen rays in radiotherapy are:

1. the possibility of radical treatment of malignant tumours which are only accessible with difficulty by other techniques,
2. the ease of obtaining in such cases a high ratio of the dose delivered to the region of the tumour to the dose elsewhere,
3. substantial reduction of the integral dose per unit dose at the tumour, and hence of radiation sickness and general effects, and
4. the possibility of simplification of techniques of treatment including the use of single field methods.

The most important disadvantage of 30 MeV_p roentgen rays in radiotherapy appears to be that clinical control of the treatment is in general very difficult because the maximum tissue reactions occur in the depths and are usually not visible. The skin reactions are mild and bear no obvious relation to the reactions of the deep tissues. The reality of this difficulty was evident in the treatment of the case of carcinoma of the soft palate with extension to the lateral pharyngeal wall (Case 2) in which there was an extremely severe reaction in the region of the palate and fauces, while the skin showed only a slight erythema on the entrance side and a dusky erythema on the exit side. The observed distribution of the tissue reactions is exactly as expected from the measured isodose curves. With 30 MeV_p roentgen rays, there is greater need than ever before of the most careful clinical management of the patients undergoing radiotherapy.

Most of the treatments which we have carried out were with dose rate 8—11 "r" per minute in the filtered beam at F. S. D. 100 cm.

This dose rate is practicable. However, when it falls below 5 "r" per minute the treatment times become rather long and the reduction in the number of cases which can be treated becomes a factor limiting the use of the 30 MeV synchrotron in clinical trials.

At present, the main disadvantage of the machine is its unreliability but presumably this difficulty will be overcome in the course of time.

The fixed beam is inconvenient. The noise of the machine is less than was expected and does not appear to be a disadvantage. The present equipment is limited to irradiation of a volume of tissue not greater than a 7.5 cm diameter sphere until the dose rate can be increased to enable the use of longer working distances.

After the single field technique, the next step is the assessment of the technique of two opposing co-axial fields and of combinations of pairs of such fields in the treatment of more deeply situated malignant tumours. The potential usefulness of these methods with 30 MeV_p roentgen rays is evident from the measurements of the depth doses. It is interesting to compare the approximate and inevitably rather inaccurate values of the ratio of the maximum central dose to the total surface dose for two opposing co-axial circular fields of diameter 7.5 cm at separation 20 cm with F. S. D. 100 cm for roentgen rays of energies between 2 and 30 MeV_p. The value of the ratio increases from about 1.0 at 2 MeV_p to about 1.8 at 15 MeV_p and then more slowly to about 2.1 at 20 MeV_p, reaching a maximum of about 2.3 in the region of 25—30 MeV_p. Taking into account our own depth dose measurements at 27—33 MeV_p, it is evident that as far as dose distribution is concerned there is little advantage for the case of techniques based on opposing co-axial fields in using roentgen ray energies higher than 25 MeV_p and only a small improvement above 15 MeV_p. Again, for non-co-axial cross-fired fields, there is probably little advantage in using energies higher than 15 MeV. For single field techniques, it appears to be undesirable to use energies less than 25 MeV_p and 30—35 MeV_p is slightly preferable; however, the scope of application of single field techniques is very limited.

The tumours in which it seems likely that 30 MeV_p roentgen therapy will be of value include:

1. cerebral and other intracranial tumours,
2. carcinoma of the tongue especially of the posterior third,
3. carcinoma of the naso- & oropharynx, and carcinoma of the palate,
4. carcinoma of the hypopharynx and post-cricoid carcinoma,
5. tumours at the base of the skull, especially those involving bone,
6. tumours of the middle ear,
7. tumours of the parotid gland,

8. a few cases of carcinoma of the breast, for post-operative roentgen therapy of the region of the apex of the axilla in unusually large patients,

9. possibly carcinoma of the oesophagus in the region of the middle third,

10. some cases of carcinoma of the bronchus which are inoperable on the basis of proximity to the carina but are otherwise still localised,

11. possibly, some cases of carcinoma of the uterine cervix, in stage IV, especially with bladder involvement, and in Stage III with isolated pelvic metastases, in conjunction with radium therapy, and perhaps also in Stage III, vagina,

12. possibly, some cases of advanced carcinoma of the bladder especially with invasion of the muscle.

It is concluded that 30 MeV roentgen radiation promises to be useful in the radical radiotherapy of some malignant tumours which cannot be satisfactorily treated by other methods. The depth dose distributions and isodose curves have been measured with reasonable accuracy. We must now treat and observe many more patients.

Acknowledgements

We wish to express our gratitude to the Medical Research Council for the provision of the synchrotron and the associated laboratories, to the British Empire Cancer Campaign for the award of a Junior Fellowship to D. J. A-W., and to the British Council for the award of a Scholarship to R. B.

We wish to acknowledge the skilled assistance of Mr. R. J. S. Stearn and Mr. C. M. Rawlings in the operation and maintenance of the synchrotron, and of Mr. V. D. Martin in the construction of much of the ancillary apparatus.

SUMMARY

The paper is an account of the beginning of the clinical use of the 30 MeV synchrotron in radiotherapy. The problem of relative biological efficiency is considered from the practical point of view of dose levels likely to be required.

An account is given of 3 illustrative cases treated by means of 30 MeV_p roentgen therapy and comparison is made with conventional radiotherapy.

The advantages and disadvantages of 30 MeV_p roentgen therapy are discussed.

ZUSAMMENFASSUNG

Der Aufsatz enthält einen Bericht über den Beginn der klinischen Anwendung des 30 MeV Synkrotrons in der Radiotherapie. Das Problem der relativen biologischen Effektivität wird vom praktischen Gesichtspunkt der wahrscheinlich notwendigen Dosisgrenzen betrachtet.

Es wird ein Bericht über 3 illustrative Fälle abgegeben, die mit Hilfe der 30 MeV_p Maschine röntgenbestrahlt worden sind; ein Vergleich mit der konventionellen Radiotherapie wird angestellt.

Die Vor- und Nachteile der 30 MeV_p-Röntgentherapie werden diskutiert.

RÉSUMÉ

Cet article rend compte du commencement de l'utilisation clinique en radiothérapie du synchrotron de 30 MeV. La question de son efficacité biologique relative est envisagée du point de vue pratique de l'importance des doses vraisemblablement nécessaires.

Trois cas traités par la roentgenthérapie à 30 MeV_{max} sont présentés à titre d'exemple et la comparaison est établie avec la radiothérapie ordinaire.

Les auteurs étudient les avantages et les inconvénients de la radiothérapie à 30 MeV_{max}.

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ERRATUM

Part I (October 1953) Fig. 5, on page 428.

The measurement on the extreme right of the figure shold be 19.3 *mm*, not *cm*.

BOOK REVIEW

La Colangiografia Laparoscopica (Colangiografia no Quirurgica). By M. Royer. 172 pp, 79 illustrations. Libreria "El Ateneo" Editorial, Buenos Aires 1952.

Laparoscopic cholangiography means a filling of the biliary ducts after laparoscopy without laparotomy. Since 1940 the author has obtained a filling of the biliary ducts in this way in more than 400 cases. The gallbladder was punctured with a needle passed through a fairly fine (5 mm outer diameter) laparoscope. The contrast medium used was of the diodone type.

A filling is usually obtained of the gallbladder, of the ductus cysticus and ductus choledochus and the contrast medium passes out into the duodenum. In addition to these anatomic topographic relationships, cholangiography gives information of physiologic interest, such as the emptying of the gallbladder. This occurs without peristalsis and without any change in its shape. Neither did the author observe any contractions of the ductus choledochus. His studies therefore support the view that the contractions demonstrated by other workers in this field were attributable to the fact that they used iodized oils.

This form of cholangiography may, of course, also demonstrate stones present not only in the gallbladder, but also in the deeper biliary ducts. The author stresses that it is just as important to visualise the ductus hepaticus and its branches as it is to demonstrate stones in the bile duct. However, judging by the illustrations given, these first-mentioned ducts are by no means always filled. The author is of the opinion that in normal subjects no filling of the hepatic branches is obtained, the contrast agent meeting less resistance in its flow into the duodenum. This limits the value of the method considerably, especially in view of the fact that, as the author himself points out, hepaticus-choledochus stones may be present without demonstrable "hypertension of the sphincter of Oddi", and then the ductus hepaticus is normally not filled.

Much space is given not only to the discussion of hypertension, but also to conditions classed as choledochitis and odditis. It is difficult to judge from the report whether these diagnoses are justified.

In tumour cases cholangiography proved very useful in the demonstration, localisation and assessment of the severity of any obstruction.

Laparoscopic cholangiography thus appears to provide a tool capable of giving valuable information preoperatively. However, its reliability cannot yet be compared to that of operative cholangiography. The value of the method is also limited by the fact that it cannot always be performed. Of the last 200 cases technical failure occurred in 23, and in 29 the examination could not be concluded because of gross pathologic anatomic changes.

Olof Norman.

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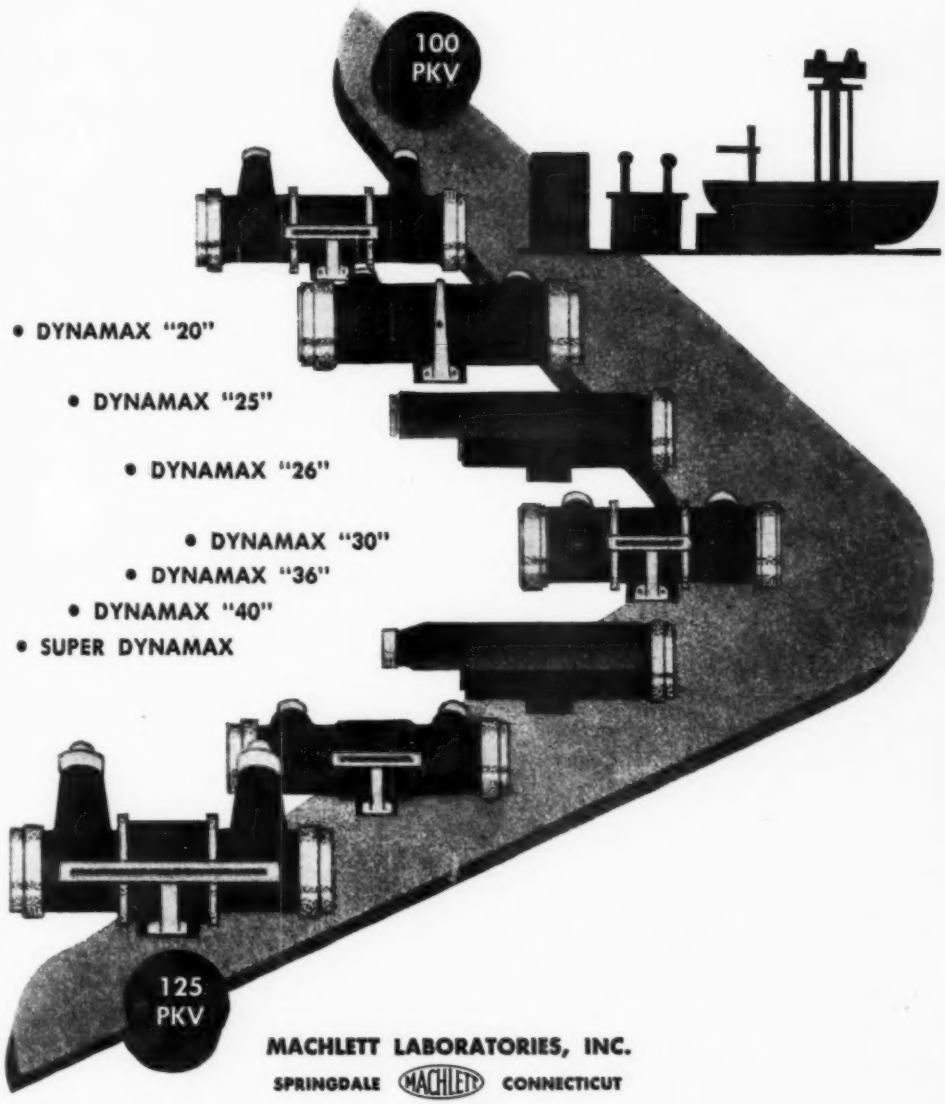

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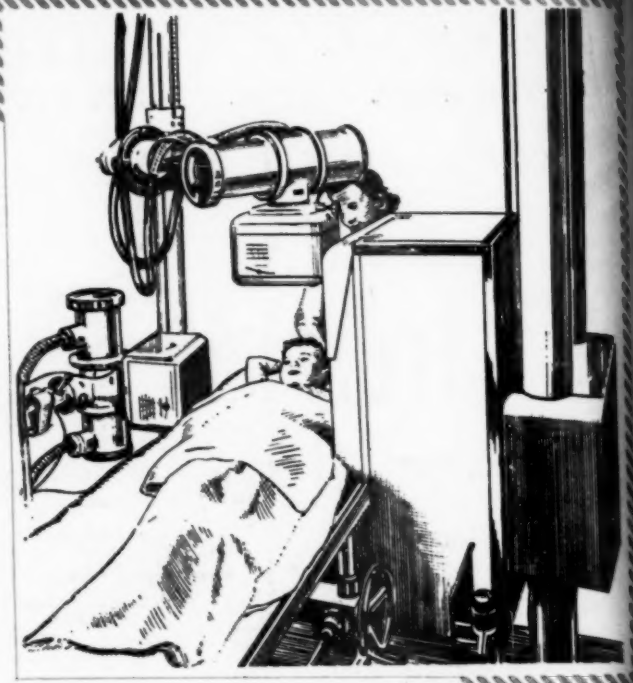

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